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ADDRESS OF THE PRESIDENT

PROBLEMS IN THE TRAINING OF THE SURGEON*

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FORTY-FIVE YEARS AGO Professor William Stewart Halsted gave an address at Yale University entitled "The Training of the Surgeon." This was one of his few addresses of a non-technical nature. At that time Halsted was 52 years of age and had been chief surgeon of the Johns Hopkins Hospital for the 15 years since its opening. He had already exerted a lasting influence on surgery by his work on local and regional anesthesia, on intestinal suture, on the treatment of hernia and of carcinoma of the breast, on the use of non-absorbable suture material and also by making other important contributions. He had already trained men—Cushing, Bloodgood, Young, Mitchell, and others who were to become leaders. He was intensely interested in the training of surgeons, had carefully studied such programs during his various visits to Europe, and he considered this subject in detail in his Yale address. His dissatisfaction with the situation in this country is shown by the following statement: "Although we have in the United States several (five or six) moderately well-endowed medical schools with a university connection, the problem of the education of our surgeons is still unsolved; our present methods do not by any

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means suffice for their training. Do we require stronger proof of the inadequacy of these methods in producing young surgeons than is presented by the so-called sacrifices which our young men today are willing, nay, most eager, to make in order to obtain a training which seems even to them not only desirable but absolutely essential for success of a high order?" Having asked this question, Dr. Halsted proceeded to describe the organization of the surgical house staff in the Johns Hopkins Hospital where the plan was widely different from that which existed elsewhere in this country.

His description was as follows: "The surgical staff consists of nine men, eight internes and one externe. The externe is an assistant in surgical pathology. . . . Four of the internes serve for one year, only the honor men of each class at graduation being entitled to these positions; but the permanent staff, so-called, consists of four men, the house surgeon and three in line of preferment. Men from any part of the country, if they have had the proper training, are eligible for the permanent positions. Great care is exercised in the filling of the vacancy on the permanent staff, which occurs once in two or three years, and advancement is not guaranteed to the appointee. The House Surgeon's term of service is still optional. He receives a salary; the other assistants are not paid. The assistants are expected, in addition to their ward and operating room duties, to prosecute original investigations and to keep in close touch with the work in surgical pathology, bacteriology, and so far as possible, physiology."

Dr. Halsted's interests were not restricted to the training of general surgeons but were extended to the various special fields. His policy here, as in the selection of his own residents, was to choose the best young surgeon available and to place him in charge of the special field in question. Thus Cushing, and later Dandy, were asked to head the Division of Neurosurgery, and similarly Young was put in charge of Urology, Baer of Orthopedics, and Crowe of Otolaryngology. In most instances the head of the division was given a free hand in the selection of his associates and in the development of his field. The number of outstanding specialists who were thus trained is testimony to the excellence of the system. In fact, the special fields in Dr. Halsted's clinic were as successful as the parent department in their contributions to knowledge and in the training of leading men.

The advantages of the residency system are obvious to all who are familiar with it. It provides a graduated responsibility in the course of the training until, at the completion of his tenure, when still under nominal supervision, the resident has independently treated a considerable number of patients suffering with the most serious conditions in his field. At the same time, having for years been carefully taught and closely supervised by his seniors, he has had increasing authority in instruction of his juniors and the delegation of clinical responsibility to them. A good, well-established residency system means that the patients receive proper care; it means that the senior staff have dependable assistance in the operating room and in the preoperative and postoperative care of their patients; it means that the medical students and nurses

have good supervision, and it means that everyone is on the alert to keep abreast of advances in knowledge and to make new discoveries, since there is no better stimulator than the keen young house officer. A good residency system transfers the university atmosphere to the wards of a hospital.

The successful functioning of the plan was, and still is, dependent upon the selection of good house officers, the delegation of proper authority to them, and their interest in teaching one another. It seems so simple, and it was so successful from the beginning, that it is difficult to understand why general acceptance of the plan was so slow. The most likely reason is that the chief of service and his associates were not so convinced of the value of this type of residency that they unselfishly allocated the clinical material to the residents. These men must be willing to advise and assist in the care of the ward patients, but must not take over except in unusual circumstances. Members of the upper staff can do serious harm to the residency system if they appropriate and operate on the more interesting ward patients. The permanent staff also must be sufficiently interested in teaching and in the advancement of surgery to be willing to welcome further competition, for it must be realized that some of the graduates of the residency system will remain and practice in the locality where they received their training.

If it required eight years to train a surgeon in 1904, how long should it require today when one considers the enormously increased scope of surgery? A study of the operative schedules of that period shows that most of the operations were incision and drainage of abscesses, appendectomies, herniorrhaphies, amputations of extremities, operations for osteomyelitis, cholecystostomies, and exploratory laparotomies. The field today has widened greatly and is still growing; however, the fundamental principles in diagnosis and operative treatment have not altered too much and they were as difficult to acquire then as now. In fact, advances in fields such as radiology have resulted in the earlier diagnosis and more accurate localization of lesions and have made surgery easier in many respects. This fact leads one to ask whether it should require eight years to train a surgeon at the present time. Obviously the period will vary according to the ability of the candidate and the adequacy of the clinical opportunities. I agree with Dr. Edward Churchill that an excellent surgeon could be trained in a much shorter period of time if everything revolved around the training of this one man. This would mean that others who were to be excluded from the residency would have to perform most of the less interesting work connected with the running of the surgical service. Furthermore, it would mean that the outstanding young resident with this intensive but abbreviated training would miss some important steps and would lack maturity. The major defect, however, would be that this plan would not be conducive to the training of the younger men by the resident and one of the best features of the residency system would be lost. The assistant resident who has received instruction and advice from his resident feels it an obligation and a pleasure to pass this information on to his associates when he in turn becomes resident. In summary, it is difficult to visualize even under ideal circumstances an adequate training in

general surgery in less than five or six years from the time of graduation from medical school. This period is certainly a minimum if the trainee is to spend any significant amount of time in experimental work, in surgical pathology, and in teaching. I regard it as very important that the surgeon in training should devote a year to investigative work, preferably in one of the basic sciences.

There is an unfortunate financial problem usually associated with the long training period. If the finished product of the residency has spent four years in college, four years in medical school and six years in a residency program, it is obvious that he is not self-supporting for at least 14 years after the completion of his high school studies. By the time the candidate has finished this training, he is certainly in the early thirties. His schooling from the high school period to the completion of training has probably cost him in the neighborhood of $20,000. If the institution with which I am associated is representative, his total salary during six years as a house officer will be about $2000, leaving a deficit of $18,000. A consideration of this financial problem led Dr. Churchill a few years ago to express the hope that some means might be found to balance the lean and the fat years in a surgeon's career. The so-called fat years, however, have lost some of their obesity as a result of high income taxes. To state the problem more concretely, why should a 30-year-old assistant resident in surgery have a salary of only $200 a year when the surgeon of 50 has a large gross income, the major part of which is, however, subject to heavy taxation? Should not some way be evolved whereby the surgeon in training would receive a living wage and would not be heavily in debt at the time he begins to earn a livelihood in the practice of surgery? The problem is a difficult one. Possibly the successful surgeons in various hospitals might create a foundation to which they would allocate a certain percentage of their earnings on a tax exempt basis for the support of young surgeons in training. There would be some loss to the internal revenue department, but the benefit to surgery would be great.

A difficult decision confronts the graduate of the residency system in a hospital connected with a medical school. If a position is available, should he remain at the institution in which he has received his training and set as his goal a career in academic surgery? In favor of this decision is the fact that the university atmosphere is pleasant and stimulating. Opposed is the rather poor financial return and the scarcity of good academic positions at a higher level. One should not choose this type of career unless he is interested in research. If the graduate is not interested in an academic career, or if a position is not available, how is he to decide where to practice his profession? The fact that a medical school and teaching hospital are at hand and that he will probably be able to maintain some connection with them tempts him to remain in the city in which he received his training. Furthermore, he will have had pleasant associations with many members of the profession during his training and these will be helpful. On the other hand, the number of surgeons per unit of population is usually higher in such medical centers. The portion of the com-

munity served by the university hospital is already adequately supplied with good surgeons and it is difficult to develop a large practice. It is my impression that there are some excellent surgeons in medical centers who are not particularly busy. Therefore, should not the well trained surgeon be encouraged to go to a community in which there are fewer such men and where probably he would render a more needed service? Despite the fact that the well trained surgeon may have difficulties in adjustment at the beginning, I think that those of us who have the privilege of training residents should advise some of them to locate in cities which are not so-called medical centers. It is part of our duty to encourage a better distribution of good surgical care. At the same time it is probably our greatest obligation to foster research and teaching, and the occasional surgeon with exceptional abilities along these lines should be given an opportunity in a university hospital and medical school.

Probably the most important years for those interested in academic surgery are the first ones subsequent to the completion of the residency. Whereas many of Dr. Halsted's residents were offered important positions elsewhere almost immediately after finishing their training, the situation has now altered greatly because of the establishment of good residencies in many places and the ensuing keener competition. Important positions in academic surgery are usually awarded now, not to graduating residents, but to those who maintain a close connection with a teaching hospital in the post-residency period. This period should be one in which the individual has ample time for research and teaching and a small but adequate number of patients to permit him to advance further his knowledge and skill in clinical surgery. Unfortunately there are too few places in which such opportunities are available.

I come now to the central theme of this discussion—a consideration of the problems that may imperil the training of the surgeon of the future. These problems are no fault of the candidates themselves. There are more excellent men desirous of training than there are suitable positions, and the applicants are willing to work long and hard without compensation if given the opportunity. The first problem is the increase in the cost of hospital care and the likelihood that hospital deficits will result in a restriction of admissions to the ward services in teaching hospitals. The second problem is the effect of the changing pattern of medical practice on the training program. While the two are closely related, they had best be considered separately.

There are many reasons for the increase in the cost of running a hospital. Among these are devaluation of the dollar, increase in salaries, decrease in working hours, increase in the cost of food and supplies, and the expense incident to the application of many advances in medical knowledge. Two men are necessary to replace the faithful old orderly who would work 80 hours a week. The long hours imposed upon general duty nurses of earlier days are now paid for as overtime. In the name of higher education the student nurse contributes less to patient care. Almost every advance in medicine adds to the cost of medical care. Notable among these are the employment of chemotherapeutic and antibiotic agents and the copious use of blood and

blood substitutes. As a result of these and other advances the scope of surgery has been extended greatly, and more difficult, more expensive and more prolonged procedures which require excellent anesthesia and costly preoperative and postoperative care are now being performed. The expense item which has altered least is the house officer. His room and his food cost the hospital more but his salary remains about the same, which is practically nil. The house officer is the one individual who has not shared in the increased expenditure of money by the hospital and yet it is his training which will suffer if admissions to the hospital wards are curtailed because of financial difficulties.

Before leaving this economic problem, it might be interesting to mention in a general way some of the problems connected with the hospital with which I am associated. This is pertinent because the Johns Hopkins Hospital is fairly representative of the teaching hospitals and was instrumental in its early years in initiating the residency system in this country. Sixty per cent of the patients are ward patients, a proportion which is roughly what it has been from the beginning. During the past nine years the expense of running the hospital has increased by more than 300 per cent. Salary items for the non-medical personnel have increased by 400 per cent. Other expenses have increased by more than 200 per cent. The income from endowment has not increased. The contribution of the city and the State to patient care has been considerably increased but not nearly enough to meet the cost. There is a long waiting list of private and semiprivate patients and there is always the temptation to reduce the ward population in favor of those patients who can bear the full expense, but this course should not be followed in a university hospital which was established primarily for teaching and research and the care of the ward population. The residency training program has suffered in similar institutions in which the ward services have been curtailed. I hope the answer to our problem will be neither governmental control nor conversion to the status of a strictly private hospital.

The second point is the effect of the changing pattern of medical practice on the residency system. Worthwhile plans such as the Blue Cross have already reduced slightly the ward population. The medical care plans for war veterans and those of large industrial corporations and unions have had a similar effect. It is not possible to predict accurately what final plan or legislation will evolve from the number of medical aid plans proposed or the various forms of legislation under consideration—voluntary insurance, compulsory insurance, private, state or federal administration. These various plans all have the common denominator that they furnish to the voluntary or involuntary participants some method for part or full payment to the physician for medical care. The ward service and the residency system have been built upon the principles of providing free medical care for those of the ward population who do not choose their own physician, and placing the responsibility for such service on the department head and the resident staff of the hospital. It is obvious that abolition of the principle of free medical service would seriously

affect both the ward service and the residency system. This is particularly true in the various surgical fields where a large volume and variety of clinical material are necessary for proper training. A number of residents in the non-operative fields can profitably study the same patient, but after all, only one surgeon can perform the indicated operation. Doctor Edwin Lehman stated recently, "Unless . . . some method is devised whereby a part of the surgically sick can be assigned to the care of properly chosen and supervised residents in training, we may wake up to a situation in which no adequate training is possible."

The residency system in the teaching hospital has functioned effectively in the past because (1) there has been adequate clinical material, (2) the staff has been able, when beds are limited, to select the more instructive cases for admission to the hospital, and (3) to the resident staff has been delegated the responsibility, under supervision, of caring for the patients. It is pertinent to ask how a new pattern of medical practice will affect the existing residency system. First, how will it affect our ward population? The present ward population is derived from three main sources: (a) from indigent patients who come of their own volition to the out-patient department, (b) from patients in the low-income brackets who are referred by their personal physicians, and (c) from patients with difficult diagnostic or therapeutic problems who are referred to the teaching hospital because of its unusual facilities. If, under some insurance plan or legislation, free choice of a surgeon (with guaranteed fee) is offered to those in the group now cared for on the wards, it is likely that a much smaller number of patients will apply for the ward service, and this reduction must of necessity affect adversely the population of the public wards. This would be a loss to the patient as well as to the teaching service, since professional care on the wards is as good as or better than that obtainable under other conditions. It is the professional fee rather than the hospitalization payment that introduces the most difficult problem. It is readily conceivable, in order to obtain patients to fill the ward beds, that the teaching hospitals may be forced to enter into contracts with private insurance companies or some governmental agency for the provision of medical care to the sick in the indigent and low-income groups.

Secondly, if, in order to obtain patients to fill its ward beds, the teaching hospital enters into a contract to provide medical care, what will be the basis for the selection of patients for admission to the wards? Under any prepayment or insurance plan the private physicians or contracting institutions will probably be swamped with patients with various minor ailments or infirmities which were endured cheerfully as long as some expense was involved in seeking medical aid. This appears to have been the case in England. How can the hospital continue to select the good teaching material for admission to its wards and not be overwhelmed with excessive numbers of the less instructive medical and surgical conditions when it is under a contract to provide medical care to the insured group? How, under some of the proposed plans, can an adequate proportion of admissions of the interesting teaching cases be assured?

Furthermore, how can the interests of the severely ill patient be protected if all available hospital beds are occupied by those with minor ailments?

Thirdly, what will be the effect of a new pattern of medical practice on the responsibilities for patient care that are now assigned to the resident staff? What is the alternative if the teaching hospital refuses to compete with private physicians and does not enter into a contract for the care of the sick in the indigent and low-income groups? In order to fill its beds the hospital will have little choice except to open the public wards to all of the staff who have visiting privileges, as is now done in the private and semi-private accommodations. If this is done, how can we preserve for the resident staff the responsibility for proper medical care of the patient and how can we provide the necessary experience in operative surgery for those in training? A satisfactory solution to all of these questions will undoubtedly call for unselfishness and generosity and cooperation on the part of the entire professional staff of the hospital. Furthermore, the medical profession at large could aid greatly by continuing to refer some of the more interesting cases to the university hospitals with the understanding that care would be provided under the direction of those in charge of the residency training program. If hospitalization costs were met by governmental agencies and if there were not a compulsory professional fee, the problem would not be difficult. It is the possibility of the compulsory fee that is likely to constitute the greatest impediment to the training of the young surgeon. If there should be a compulsory fee, I would hope that the medical profession and the insurance or governmental agency involved would be willing to have fees derived from ward patients used for the support of postgraduate medical education. Because of the relatively small proportion of hospital beds available for residency training, the financial loss to the medical profession would not be great.

These are only some of the problems confronting the teaching hospitals and the residency system because of current financial difficulties and a threatening new order of medical practice. There are probably many other implications of an insurance program or of legislation for the care of the sick in the indigent and low-income groups which will seriously affect the teaching programs. Not only the training of house officers but the instruction of medical students is endangered. I confess that I have no ready answer to the perplexities of the present economic situation or to the many difficult problems that will have to be met if and when a new pattern of medical practice is adopted. Since the residency system is responsible for much of the progress that has been made in the care of the sick, the public as well as the medical profession should make every effort to preserve its essential features.

ACUTE ARTERIOVENOUS ANEURYSM OF RIGHT COMMON CAROTID ARTERY AND INTERNAL JUGULAR VEIN*

TRANSPLEURAL APPROACH TO CONTROL THE ARTERIAL SUPPLY

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THE FOLLOWING CASE of a patient with an arteriovenous aneurysm (varicose aneurysm) of the right common carotid artery and internal jugular vein, producing an acute emergency, presented several unusual clinical, pathologic and surgical features which would seem to justify its report. The aneurysm, which was associated with an unorganized hematoma of three weeks' duration, was only five weeks old when it ruptured, filling the entire right side of the neck with a hematoma the size of a grapefruit (Fig. 1) producing a surgical emergency. The case is of additional interest because of the rarity of rupture of a varicose aneurysm as well as because of the *impossibility of a direct surgical approach upon the aneurysm without massive and probably fatal hemorrhage.* Moreover, there was no appreciable cardiac dilatation or hypertrophy (Fig. 2), although the total blood and plasma volumes were definitely increased. Finally, the case is presented in the hope that the surgical approach employed may be of help to others confronted with similar cases.

REPORT OF CASE

G. V., a white boy, age 17 years, was admitted to Foundation Hospital, June 27, 1948, for treatment of a pistol wound of the right side of the neck with moderate swelling at the site of the wound. Three weeks prior to admission the patient accidentally shot himself while loading a .38 calibre pistol. The bullet entered his neck on the right side just anterior to the anterior border of the sternocleidomastoid muscle, passed through the junction of the upper and lower thirds below the cricoid cartilage, and made its exit at a level with the point of entrance. The osseous tissue was spared. The wound, which bled copiously, was not painful although there was a burning sensation in the neck. Pressure was immediately applied to the bleeding point and the patient was rushed to the hospital, by which time the bleeding had stopped. In the hospital the patient noticed that his voice was slightly hoarse and his right arm was difficult to move. He could feel a mass in his neck. Moving his neck, especially to the right, was difficult and painful. He was told that he had a hematoma in the right side of his neck about the size of an orange. The overlying skin was bluish-black in color. The administration of transfusions and penicillin and the use of a compression bandage resulted in rapid recovery and the patient was discharged in good condition five days following the accident.

The swelling in his neck gradually decreased from the size of an orange until it was about the size of a lemon. The hoarseness quickly subsided and the weakness in

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his right arm rapidly diminished. However, the patient could feel a peculiar vibration of the swelling with his hand and he could hear a buzzing noise in his right ear. He was advised to come to the Clinic for evaluation and treatment of the hematoma.

Examination on admission to the hospital revealed a normal, healthy, ambulatory, young man with a swelling in the lower third of the neck on the right side (Fig. 1). The mass, which measured about 4 by 5 cm., was firm, slightly compressible and fixed to the deep and surrounding tissues. The skin overlying the mass was normal in texture and color, and could be moved over the mass only slightly. This was evidently due to the primary extravasation of blood and subsequent hematoma. There was a small scar at the site of the swelling, the point of entrance of the bullet, and posteriorly, on a slightly higher level to the anterior scar, was the scar of exit of the bullet. The mass occupied an anatomic position between the trachea, sternocleidomastoid muscle and clavicle in the inferior anterior triangle of the neck. The trachea was pushed slightly to the left of the midline.

Palpation revealed a minimal expansile pulsation synchronous with the heart beat. A definite and continuous thrill was transmitted to the examining hand. Auscultation elicited a continuous, loud hum or roar with systolic exacerbations. This significant and characteristic murmur was transmitted distally to the base of the skull and proximally to the base of the heart.

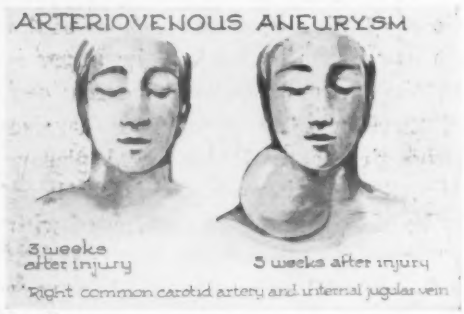

FIG. 1.—Note small size of the hematoma on the left as contrasted with large size of one on right.

Since the pulsating hematoma (pseudosac) was only three weeks old, organization, sacculation and walling off of the hematoma was only beginning. Because of the friability of the pulsating hematoma, compression and manipulation were avoided in order to prevent rupture. For the same reason, no effort was made to elicit Branham's sign.

Examination of the right arm, because of the history of muscular weakness, failed to reveal injury of the component parts of the brachial plexus. The slight weakness and pain were evidently due to traumatic and compressive neuritis of the brachial plexus. The heart and lungs were normal. The blood pressure was 140 mm./Hg. systolic and 80 mm./Hg. diastolic and the pulse rate was 104 beats a minute. A roentgenogram of the chest revealed a soft tissue mass in the right side of the neck deviating the trachea slightly to the left. Hematologic studies yielded normal results.

Because of the short duration of the arteriovenous aneurysm, incomplete organization of the periphery of the hematoma, with absence of a definite aneurysmal wall, and complete sacculation (granulation tissue only), the patient was advised to return four to six months later for treatment. He was told that he should be ambulatory but should avoid physical exertion because of the possible strain on the aneurysm (increased intrasaccular pressure) and cardiac complications (dilatation). However, he was advised to return immediately if the swelling in his neck suddenly increased in size or if he became dyspneic on walking or climbing steps. He was discharged July 1, 1948.

The patient got along well at his home in another city until the eleventh day, when the insecure pseudosac of the arteriovenous aneurysm ruptured, filling the entire right side of the neck with a large hematoma, which by stretching the tissues, compressing the brachial plexus and deviating the trachea to the left, produced considerable difficulty in breathing and pain in the neck and right arm. The patient immediately returned and

was admitted to the Foundation Hospital July 14, 1948, only 13 days after his first discharge and five weeks following the accident.

The only change in the patient's physical condition was in the mass in the neck. The patient's head was turned to the left and his chin somewhat extended, because of the large hematoma which also prevented him from turning his head to the right. The neck presented an entirely different picture from that on the first admission. The previous pulsating hematoma, which was about the size of a lemon, had suddenly increased to the size of a grapefruit. The mass, extending from the angle of the jaw down to and somewhat over the right clavicle, measured 15 by 12 cm. It was smooth in outline and quite firm to palpation. Not only did it push the larynx and trachea to the left of the midline but it compressed them as well, causing the difficulty in breathing. There was only slight pulsation of the hematoma; these meager pulsations were due to severe compression of the hematoma by the surrounding muscles and strong fascial planes of the neck. A definite thrill could still be elicited on palpation. However, it was not as sharp and intense as it was on the previous admission. Auscultation demonstrated persistence of the previous hum and murmur, but its intensity, systolic exacerbations and transmissibility were greatly reduced and limited. This was due to compression of the internal jugular vein and common carotid artery by the hematoma.

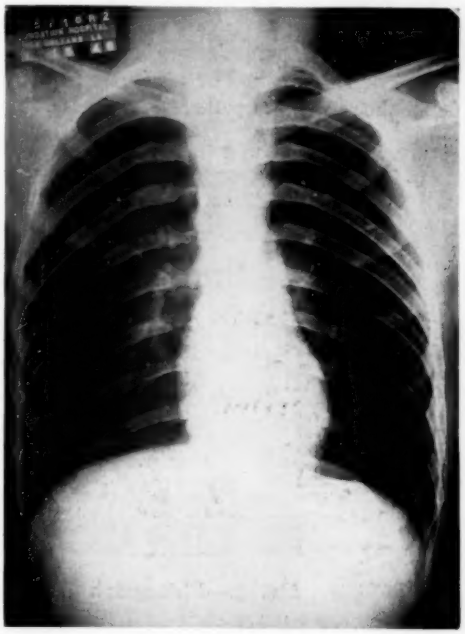

FIG. 2.—Roentgenogram of the chest taken five weeks after the accident shows normal heart and lungs and no cardiac dilatation. No change is seen from roentgenogram made two weeks previously.

The blood pressure was 140 mm./Hg. systolic and 80 mm./Hg. diastolic, the pulse rate was 104 beats a minute and the respirations at rest 20 a minute. There was slight leukocytosis.

Right auricle and arterial blood samples showed right auricle blood oxygen of 11.85 volumes per 100 cc. and 14.90 volumes per 100 cc. arterial blood. The blood volume was 6100 cc. and the plasma volume 3290 cc. A definite increase in cardiac output and an increase in total blood and plasma volume were established, but there was no definite increase in cardiac size (Fig. 2). The interval of this "auto-arteriovenous transfusion" was not sufficient to produce cardiac dilatation and hypertrophy. The pressure on the venous return channel (internal jugular vein) probably prevented the maximum total augmented arteriovenous blood volume from reaching the right side of the heart. Even though the fistulous communication was of a sufficient size, the large hematoma, with its disturbing pressure effects, precluded the required volume to produce the expected systemic or cardiac effects.

The patient was comfortable for the next two days, but the swelling in the right side of his neck was gradually increasing in size. This indicated clearly that blood was being pumped continuously into the tense hematoma and was distending the tissue of the right side of his neck. The large hematoma extended over the midline and down over the clavicle.

The patient noticed increasing difficulty in breathing. Moreover, the pain in his neck and right arm had recurred and was more severe. In view of the patient's condition, early intervention was considered imperative. It was hoped that the large hematoma, which was producing tremendous pressure upon the vital structures in the neck, could be removed. However, a serious problem confronted us. A surgical approach had to be selected which would permit exposure and correction of the arteriovenous fistula but which would also make it possible to control or prevent massive hemorrhage. The best approach is usually the one that provides direct exposure of the vessels which form the arteriovenous aneurysm. Exposing the arteries and veins just above and below the fistula, and using temporary occlusive methods produces a dry field.

The direct approach was impossible because the large hematoma would have to be incised and this would result in uncontrollable massive hemorrhage and probably profound shock with its pathologic sequelae. To assure a dry operative field (so necessary

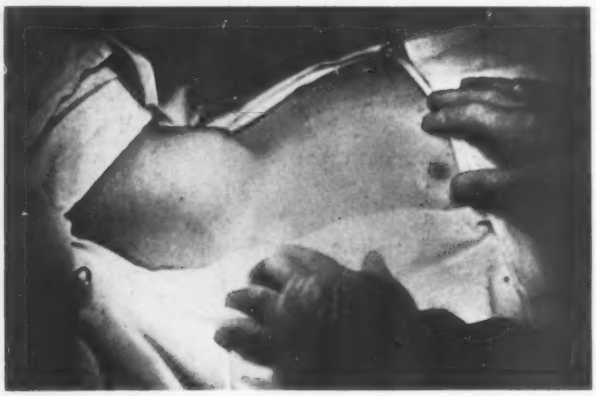

FIG. 3.—Photograph demonstrates the large hematoma and the draped field of the operation.

in the neck because of the extensive infiltration of blood of all tissues and vital structures), it would be necessary temporarily to control the proximal and distal blood flow to the aneurysm completely outside of the operative field. The plan adopted was first to control the arterial supply by using a provisional occlusive ligature upon the innominate artery as it leaves the arch of the aorta. The next objective was to control the venous return flow by a permanent occlusive ligature of the internal jugular vein between the mastoid process and the angle of the jaw. It was concluded that with the arterial supply cut off one could risk a direct approach of the jugular vein at the superior pole of the hematoma, even though the hematoma were entered. With both arterial and venous blood supplies cut off the entire hematoma could be incised, the clots rapidly removed, the injured vessels completely exposed and either their continuity restored or the component vessels ligated.

This plan was carried out on July 16, 1948, with most gratifying results. The entire neck and chest were prepared and draped (Fig. 3). An incision was made over the right fourth rib extending from the midsternum towards the anterior axillary line. Division of the muscles in the line of the rib exposed the rib periosteum. The fourth rib was exposed and resected (about 15 cm.) subperiosteally. The internal mammary vessels were doubly ligated and severed. A small incision, made through the bed of the rib into the pleural cavity, permitted the lung to collapse slowly. The pleural cavity was then opened widely. The cartilage of the second rib was transected. The wound and

the ribs were widely separated with rib spreaders. An incision was made in the mediastinal pleura and by sharp and blunt dissection the superior vena cava was exposed and gently pushed posteriorly. The lateral edge of the thymus (which seems to be quite large) was dissected up and retracted medially with a narrow Deaver retractor. By blunt dissection the innominate artery was exposed as it came off the arch of the aorta. There was a small branch that came off the innominate artery and entered the mediastinal structures. A half-curved forceps was placed around the innominate artery and a rubber dam tube 1 cm. wide was pulled around the artery. A right angle forceps was opened, the rubber dam tube passed between the blades, and the clamp then gently closed without locking. The jaws were placed against the artery, and the rubber dam ligature was tightened until the arterial blood flow was stopped (Fig. 4). The forceps was then clamped tightly and locked. This completely cut off the blood flow through the innominate artery and its branches.

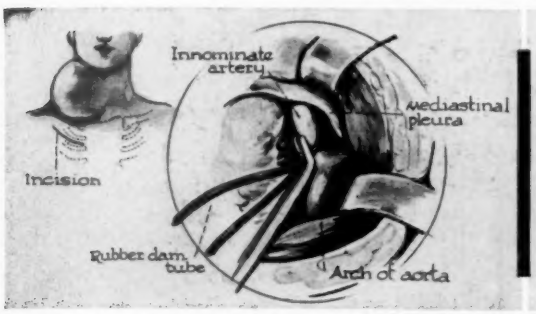

FIG. 4

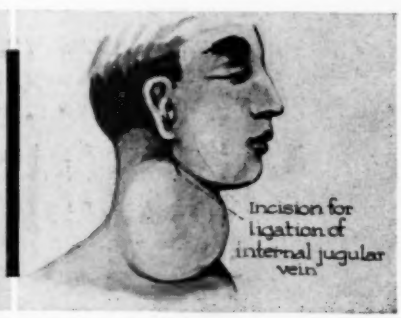

FIG. 5

FIG. 4.—Drawing shows the thoracic wound through the bed of the fourth rib. The temporary non-traumatic rubber dam ligature is seen obliterating the lumen of the innominate artery as it arises from the arch of the aorta.

FIG. 5.—Drawing shows the large hematoma and the incision behind the angle of the jaw, where the internal jugular vein was exposed and permanently ligated. When the incision was made, blood clots exuded into the wound.

Next, the lung was inflated to full capacity. The rib spreaders were released and the thoracic wound was covered with gauze packs after fixation of the forceps that held the temporary occlusive rubber dam ligature. An incision was made along the median border of the sternocleidomastoid muscle between the angle of the jaw and the mastoid process in order to expose the internal jugular vein (Fig. 5). This incision was just slightly above the upper pole of the large hematoma. When the incision passed through the skin, platysma muscle and cervical fascia, clots from the large hematoma exuded into the wound. It was immediately seen that the large hematoma had been entered. A gauze pack was introduced into the wound against the hematoma and a retractor forced the gauze pack against the hematoma to prevent escape of more clots into the wound. The internal jugular vein was easily exposed and a silk ligature placed around the vein and tied tightly. The return central venous flow was thus abolished. With both the arterial and venous blood flow completely under control the incision was extended down to the clavicle so that the large hematoma came into view (Fig. 7). With one sweep of the hand the hematoma was removed from the wound. The rest of the clotted blood was easily removed with gauze sponges. The common carotid artery and internal jugular vein were completely exposed (the surrounding tissues having been dissected up by the hematoma) in the bottom of the wound (Fig. 6). Examination of these struc-

tures demonstrated that the common carotid artery had been completely severed by the bullet and the vein almost completely so by a through and through wound. There was only slight oozing from the distal end of the artery and minimal back flow from the proximal vein—an almost dry field.

The walls of the artery and vein, which were infiltrated with blood, were so friable that arterial suture to restore the continuity of the vessels could not be attempted. Therefore, the artery and vein were ligated above and below the injury (Fig. 6).

The provisional ligature was then removed from the innominate artery and the blood flow re-established. Inspection of the aneurysmal site and the cervical wound revealed a perfectly dry field. The cervical wound was covered with moistened saline gauze squares until the thoracic wound could be closed. The mediastinal pleura was closed with a running suture of fine catgut. The pleural cavity was completely free of

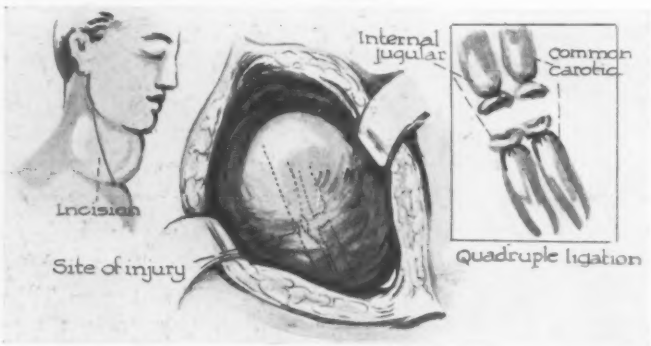

FIG. 6.—Drawing shows the large hematoma exposed by an incision extending from between the mastoid process and angle of the jaw down to and slightly beyond the clavicle. Inset shows quadruple ligation of the common carotid artery and internal jugular vein.

all blood, fluids and secretions. The lung was expanded and the thoracic wound closed in layers by interrupted cotton sutures. Before the final sutures of the thoracic wound were tied, a catheter was placed into the pleural cavity and all air aspirated as the lung was finally expanded under pressure. The cervical wound was inspected carefully for bleeders; only a few small cutaneous vessels were found and these were ligated. All the tissues of the neck on the right side were infiltrated with old and new blood. The muscles of the neck, which had been widely separated by the hematoma, were sutured back in place along with the cervical fascia. A small rubber dam drain was placed in the wound. The platysma and superficial fascia were closed with interrupted sutures of fine cotton. The skin was closed with interrupted dermal. The patient left the operating room in excellent condition.

During the operation phlebotomy was done by the anesthetist and 1000 cc. of blood was removed. After ligation of the vessels the blood was returned through the arterial route. The patient was given 100,000 units of penicillin every 3 hours as prophylaxis against infection of the cervical wound and pleural cavity. The only postoperative complication was pleural effusion on the right side. The chest was aspirated on July 19, yielding 1000 cc. of blood tinged fluid. Five hundred thousand units of penicillin was injected into the pleural cavity through the aspirating needle as a prophylactic measure. On July 27 the chest was again aspirated and 450 cc. of clear fluid was obtained (cul-

ture of the fluid in both cases was negative for organisms). Blood volume estimation 11 days postoperatively was 4680, plasma volume 2810 cc., showing a decrease of 1420 cc. and 480 cc., respectively. The patient was discharged August 8, 1948, completely cured of the aneurysm (Fig. 7).

DISCUSSION

There are several unusual features of interest in this case. In the first place, the occurrence of an aneurysmal sac in association with an arteriovenous fistula (varicose aneurysm) is uncommon. Most arteriovenous fistulas are traumatic in origin. They occur between the artery and accompanying vein. The opening between the two vessels is rapidly sealed off; this prevents the formation of sacculation in over 90 per cent of cases. It is only when both walls of the artery and vein have been penetrated, or the artery has been incompletely (partial destruction of the wall of the artery) or completely transected that a pseudosac accompanies the fistula. In the present case the artery had been completely, and the vein partially, severed. Therefore, an unorganized incompletely sacculated pseudo-aneurysmal sac accompanied the arteriovenous fistula — a true varicose aneurysm. The sac is formed by encapsulation of a pulsatile hematoma, by proliferation of connective tissue which organizes the periphery of the hematoma, resulting in a limiting fibrous wall. The blood clot within the encapsulated hematoma becomes laminated and this strengthens the wall of the pseudosac. The central portion of the pseudoliquefied hematoma becomes "honed out"; the resulting cavity is then lined by endothelium from the intima of the vessels. Thus, a pseudo-aneurysmal sac is formed conjointly with the arteriovenous fistula.

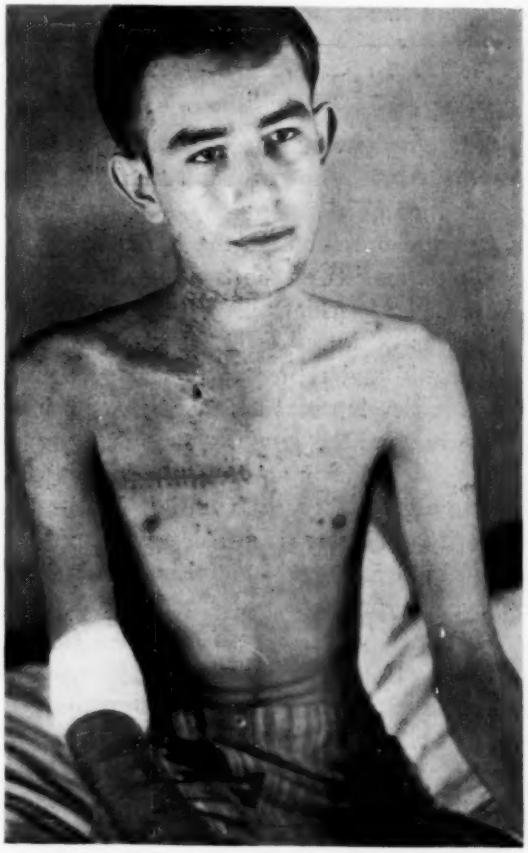

FIG. 7.—Photograph shows the healed cervical and thoracic wounds on the eighth postoperative day. The small opening seen at lower angle of the wound below the clavicle is where the drain (rubber dam tube) protruded from the lower angle of the cervical wound. It was necessary to use a drain because of the diffuse infiltration of the cervical tissues with blood.

Another interesting feature is that a varicose aneurysm seldom if ever ruptures. However, in its formative stage, before sacculation, organization and encapsulation occur, there is always danger of the unlaminated hematoma losing its tissue and muscular support with sudden blowing out of the pulsating hematoma. When this occurs, it results in formation of a hematoma the size and extent of which is limited only by fixed fascial planes and muscular attachments. If the secondary hematomas are large and under considerable pressure, they can endanger life or result in loss of a limb by pressure upon vital structures or the collateral blood supply to the periphery. If situated close to or within a cavity, they may rupture into the cavity and result in sudden death.

In the present case the large hematoma produced deviation, angulation and compression of the trachea with resultant difficulty in breathing. Pressure on the brachial plexus caused pain in the patient's neck and right arm as well as weakness of the muscles of the arm. There was also pressure upon the carotid and return venous blood flow. This pressure upon the carotids aided in development and opening of collateral circulation to the brain. The pressure upon the venous return flow prevented large volumes of blood from being shunted from artery through vein to the right heart. This phenomenon was to a great degree responsible for the absence of cardiac dilatation. In the majority of all cases in which rupture of the pseudosac of a varicose aneurysm occurs and a large hematoma develops, emergency steps must be taken to relieve the pressure and cure the aneurysm.

Another interesting phase of this case is the absence of cardiac dilatation and hypertrophy in view of the great increase in total blood and plasma volume and cardiac output. Preoperatively the blood volume was 6100 cc. and the plasma volume 3290 cc., and postoperatively the former was 4680 cc. and the latter 2810 cc.

Four factors determine the development of cardiac dilatation after the occurrence of an arteriovenous aneurysm: (1) time, (2) size of the vessels, (3) size of the opening and (4) an unobstructed venous return to the heart from the arteriovenous fistula. The time factor is dependent, to a certain degree, upon the size of the vessels and the size of the fistulous opening which accurately determines the blood volume shunt from artery to veins to heart. If the venous return from the arteriovenous fistula to the heart is decreased by obstruction of the vein involved, there will be a minimal volume shunted directly to the heart. Under these circumstances cardiac dilatation will not occur. The "autotransfusion" of arteriovenous fistula may be massive, moderate or minimal in volume, depending upon the size of the vessels involved, the size of the opening, and the distance from the cardiac chambers. If the autotransfusion is massive in volume, that is, between the aorta and inferior or superior vena cava, death rapidly supervenes because of overloading of the right side of the heart, with cardiac failure. If the autotransfusion is moderate in volume (small opening between large vessels or large

opening in moderately small vessels) and is continued over a long period of time, cardiac dilatation and hypertrophy of the cardiac muscle invariably occur. This complication will eventually cause cardiac decompensation if not corrected. If the vessels are small (radial or ulnar artery and vein) and the autotransfusion is of small volume, cardiac dilatation does not occur. In the case reported, although the vessels involved were of large caliber (common carotid and internal jugular) and the opening between artery and vein was maximum, the arteriovenous shunt did not produce cardiac effects. The reason for this is the internal jugular vein was so compressed that the maximal shunt did not reach the right side of the heart in sufficient and steady quantity to produce cardiac dilatation.

Probably the most interesting problem presented by this case was the question of the best surgical approach to relieve the arteriovenous fistula and at the same time prevent any form of hemorrhage. The large hematoma that filled the right side of the neck absolutely prevented any type of direct surgical approach because the proximal and distal blood supply could not be controlled. A direct attack without preliminary control of the blood supply would have resulted in uncontrollable massive hemorrhage, which if not immediately fatal, would have resulted in shock and its sequelae. Therefore, it was necessary to devise a surgical approach which would not only control the distal and proximal arteries and veins but would also produce a dry surgical field. The plan that seemed to accommodate the necessary requirements was: (1) to control the arterial supply through the innominate, and (2) to control the venous blood flow distal to the arteriovenous fistula. This was easily accomplished by applying a temporary non-traumatizing ligature of rubber dam to the innominate artery near the arch of the aorta and a permanent ligature on the internal jugular vein at a site behind the angle of the jaw. These two procedures turned an almost insurmountable obstacle into a simple surgical procedure. Another disconcerting factor was the possible complications of ligation of the common carotid artery. I do not believe that ligation of the common carotid artery is followed by as high a mortality or other complications as reports in the literature indicate (30 to 50 per cent). Most of these statistics are ancient. Rogers[1] reported 19 personal cases of ligation of the common carotid artery with no cerebral complications and one death. The death occurred in a patient who was practically moribund from cerebral hemorrhage (intracranial aneurysm) before operative intervention. However, one should not ligate the common carotid without first demonstrating the adequacy of a collateral circulation by all available methods. In the present case it was impossible to test the collateral circulation by temporary occlusion of the common carotid by the Matas compressor because of the hematoma. However, because of the great pressure of the hematoma upon the vessels of the neck it was surmised that the carotid flow had been greatly decreased, the collaterals had been opened up and therefore a positive degree of collateral circulation had been established.

That these deductions were correct was demonstrated by the fact that the patient had no complications following ligation of the common carotid artery.

Transpleural transmediastinal control of the great vessels of the neck at their origin can be unhesitatingly recommended in all cases of arterial or arteriovenous aneurysms of the great vessels of the neck if it is impossible to control the artery between the aneurysm and the heart. In conclusion, it can be stated that this case presented a surgical problem which at first seemed almost insurmountable, yet resolved itself into one of such simplicity that it allowed the surgeon to operate with equanimity.

BIBLIOGRAPHY

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DISCUSSION.—DR. JAMES D. RIVES, New Orleans: I would like to congratulate Doctor Gage on his extraordinary case. He has displayed all the courage and ingenuity that I have come to expect of him in half a lifetime of association. I cannot agree, however, that he has made this procedure simple. I do not believe this can be done, but he has come as near to it as possible.

I want to present an alternative method of handling arteriovenous communications in the neck in which adequate preliminary control of circulation is not possible. This is applicable only to direct arteriovenous fistulas and could not be used in the case presented by Doctor Gage. I have two examples that I would like to report.

Case 1. A gunshot wound of the upper portion of the common carotid just below the bifurcation, in which there was so much scarring proximal to the fistula that preliminary control of the arterial circulation was impossible. Preliminary control of the vein was secured by proximal and distal ligatures. The communication was then closed by transfixion sutures that picked up the margin of the arterial wall. As in Doctor Gage's case, this was not as simple as it sounds. In the course of the dissection I found to my consternation that the lateral wall of the internal jugular vein consisted of the sternomastoid muscle. Hemorrhage was profuse and was controlled only with difficulty. After the fistula was closed the ligated vein was plicated over the repaired opening as in the Matas transvenous suture. It should be noted that Matas' technic is possible only when preliminary control of circulation is complete. We believe that it is unwise to restore the continuity of the vein because it invites thrombosis, and because in the presence of an arteriovenous fistula the number and size of the collateral veins is so great that the sacrifice of the major vein is of no consequence.

Case 2. A stab wound at the base of the neck on the right side produced a direct arteriovenous communication between the first portion of the subclavian artery and the internal jugular vein. In passing, I would like to comment on the fact that arteriovenous fistulas of the subclavian and axillary arteries often do not involve the subclavian or axillary veins because of the wide separation of these vessels in the greater part of their courses. In this case I could have secured preliminary control of circulation, as Doctor Gage did, by the transthoracic approach, had it been necessary. But since I had a direct communication with a comparatively small fistula, it was possible to isolate the communication and to control it by transfixion suture exactly as in the first instance. I must repeat that this method is applicable only to those cases in which there is a direct arteriovenous communication without an intervening sac, and it is necessary only when

adequate control of the artery and vein proximal and distal to the fistula is not practicable

DR. MIMS GAGE, New Orleans (closing): I wish to thank Doctor Rives for his excellent discussion of my paper. This case was reported in the hope that the technical procedure used might be of benefit to others who may encounter similar cases. The transthoracic, transmediastinal control of the arterial supply by provisional ligature (rubber dam) of the innominate artery prevented hemorrhage and converted an almost insurmountable obstacle into one of simplicity. Otherwise, an uncontrollable and fatal hemorrhage would probably have occurred if a direct surgical approach had been used without the indirect method of controlling the blood supply.

THE CONTROL OF BLOOD TRANSFUSION HAZARDS*

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IN PRESENT DAY MAJOR SURGERY blood transfusion is perhaps next to anesthesia the most important adjunct contributing to the safety of the patient. At the present time it is not uncommon to have 4000 to 12,000 transfusions per year administered in the larger hospitals with active surgical services. The average rate in the general hospital is about six transfusions per bed per year.

Prior to Landsteiner's discovery of the blood groups[1, 2] in 1900 the chief danger of transfusions was intravascular hemolysis. So great was the resulting mortality that less than 400 transfusions were reported previous to this discovery.

With the classification of the blood groups by Jansky[3] and Moss[4] and the application of these discoveries to routine transfusions by Ottenberg and Libman[5] the demand again became large, but the difficult technic of end-to-end anastomosis, Kimpton-Brown paraffined tubes and the multiple syringe method of Linderman[6] prevented wide application. About this time a second risk was recognized when McClure[7] transmitted syphilis from the donor to the patient in using the syringe method.

Beginning in 1914 the use of sodium citrate, popularized by Lewisohn,[8] made possible the much simpler indirect transfusions, so simplifying the procedure that it was widely used in World War I.

In the early period a third and fourth risk were recognized in this stage of development, namely the reactions characterized by chills and fever and those of increasing severity and number occurring in patients receiving multiple transfusions, such as the cases of pernicious anemia, characterized by chills, fever, respiratory distress and shock. The third risk was explained by the discovery of "pyrogens" by Seibert[9, 10] in 1923. The fourth risk is probably explained by discovery of the Rh factor through the work of Landsteiner and Wiener[11, 12] and Levine and his associates.[13]

The fifth and the most serious transfusion risk next to that of intravascular hemolysis is that of homologous serum jaundice. First demonstrated by Beeson,[14] and Morgan and Williams[15] in 1943, jaundice has been recognized as a risk associated with the transfusions of pooled plasma, since there is an incidence of 4.5 to 7 per cent following its administration.

* Assisted by research grants from the Veterans Administration and the United States Atomic Energy Commission. Read before the Southern Surgical Association, Hot Springs, Virginia, December 6, 1949.

Following the original discovery of blood groups Landsteiner[2] suggested that the presence or absence of isohemo-agglutinogens in the red cells determined these groups, and the groups were named for these agglutinogens.

Group	Agglutinogens	Agglutins
AB	A and B	None
A	A	Anti B
B	B	Anti A
O	None	Anti A and Anti B

The presence of six subgroups A_1, A_2, A_1B, A_2B, A_3 & A_3B may be a serious interfering factor in blood grouping and in the use of group O as a universal donor. Usually careful grouping and the use of identical groups in transfusion cross-agglutination between donor and recipient will eliminate the possibility of dangerous incompatibilities which result in intravenous hemolysis.

An antiserum, produced when rabbits are injected with the R.B.C. of the Rhesus monkey, will agglutinate the R.B.C. of 83 per cent of the white race. Landsteiner and Wiener[11] who, in 1940 demonstrated this new antigen, called it Rh factor, believing it to be a single entity inherited as a dominant trait. In the intervening nine years at least eight antigens of this type and hence as many Rh types have been discovered.

This discovery of the Rh factor and the classification of individuals as Rh positive and Rh negative explains to a large extent at least the hemolytic disease of the newborn and hemolytic reactions that follow repeated transfusions of bloods that are compatible as far as the A.B.O. system is concerned.

DeGowin[16] with characteristic bluntness states, "It is doubtful whether any large series of blood transfusions has ever been given without hemolytic complications, some of which have been fatal. . . . Probably one to five hemolytic reactions per 1000 transfusions are inevitably caused by human error."

Although the various possible factors have been given much consideration in the etiology of hemolytic reactions, particularly the red cell stroma and the freed potassium, it is the consensus of opinion at present that the released hemoglobin is the principal element of danger, since the entire syndrome can be produced with especially prepared and preserved crystalline oxyhemoglobin.

Low potassium values in the blood may be encountered following transfusions in various conditions where there has been marked potassium depletion in the tissues as in shock, infant diarrhea, etc.[17]

Usually the first and often the most characteristic manifestations of intravascular hemolysis are chills, pain in the chest and legs, respiratory distress and shock. If the amount of hemolyzed blood is small (60 to 300 cc.), or the patient is under an anesthetic, only the fall in blood pressure may be noted.

If the first 100 cc. of blood are given slowly (15 minutes) to the unanesthetized patient under the close observation of the physician, the administra-

tion of lethal doses of incompatible blood should be avoided. Patients almost without exception survive the initial shock associated with hemolytic reactions, but the associated stagnant anoxia along with acidosis and dehydration contribute to more serious and fatal complications, that is, the so-called "lower nephron syndrome" or "renal anoxia." This syndrome is forecast frequently by hemoglobinuria, oliguria and anuria terminating with complete irreversible renal insufficiency in about half the cases.

The administration of blood to the anesthetized patient involves additional hazards more than justifying the use of plasma, albumen solutions and blood substitutes, with reconsideration and re-evaluation of the whole subject of operating room intravenous therapy.

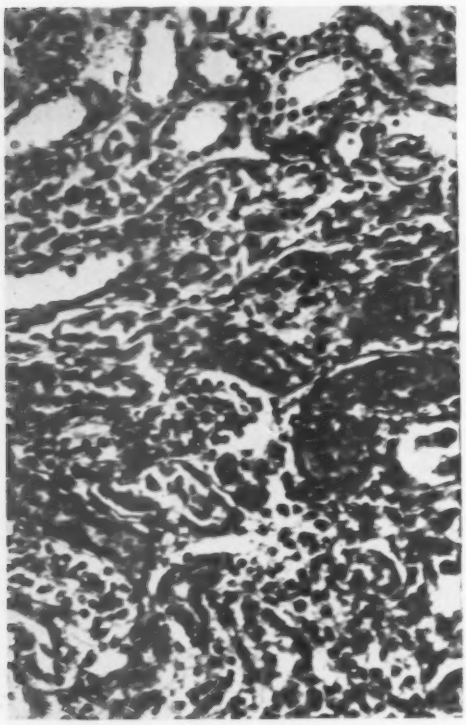

FIG. 1.—Photomicrograph, medium power, showing swelling and degeneration of the epithelium of the convoluted tubules of the kidney.

Another source of intravenous hemolysis is isoimmunization, which results from having received incompatible blood of the A.B.O. or Rh systems through an earlier transfusion and in the case of the pregnant woman from carrying a fetus of different type. This source of hemolytic reaction is small at the present time due to the careful typing in both the A.B.O. and Rh systems with cross matching of all donors and recipients.

CASE REPORTS

Case 1.—G. H., Hosp. No. 500381, Path. No. 107262, Autopsy No. 5245, was a white male, age 43; admitted August 6, 1947. Died June 30, 1949. This 41-year-old bricklayer came to the emergency room of HFH complaining of pain in the right shoulder of 3 months' duration. Chest stereos were obtained which revealed an infiltrative process in both apices. Laboratory results showed the hemoglobin to be 13.2 Gm. and RBC 4.41 million. The WBC was 14,600 with 75 per cent polys. The sputum was positive for acid-fast bacilli.

The chest roentgenograms continued to show advanced pulmonary tuberculosis of both apices with cavitation. Twenty-two months after admission a left, first stage thoracoplasty was performed under ethylene and cyclopropane anesthesia. Five hundred cc. of type O blood were given during the operation and 500 cc. of type O blood on return to his room. Both transfusions were without reaction. He did not void in the first 24 hours. The NPN rose to 82 on the second postoperative day. The CO_2 was 39.6 volumes per 100, the serum chlorides 547, the sodium was 296. The urinary output on this day was 100 cc. and examination showed the specific gravity to be 1.016. The specimen contained

4+ albumin and was mahogany-colored. The urinary output continued to be low, the NPN rose to 195, the potassium was 19.6 mg. per 100 and rose to 24.3. The patient died on the tenth postoperative day.

Autopsy showed some generalized edema. The lungs were edematous and increased in weight. The liver weighed 1700 Gm., and the usual architecture was well made out. The kidneys weighed, respectively: right 300, left 340 Gm. The cortices average 1.5 cm. in thickness, and were dark red in color. The pyramids, in contrast, were grayish-blue in appearance.

Microscopic examination showed the distal convoluted tubules having cells flattened and the lumina containing brownish granular debris or solid, brassy casts. The collecting tubules showed even more granular debris and brassy casts. There was some PMN infiltration throughout the interstitial tissue and some leukocytes within the lumina of the tubules.

The anatomical diagnosis was: postoperative state following recent thoracoplasty on the left; bilateral fibro-caseous tuberculosis; and lower nephron-nephrosis.

The almost universal use of blood stored in blood banks for periods up to 21 days adds other important possibilities of hemolytic reactions due to hemolysis of cells that takes place during storage. Factors that may be responsible are bacterial contamination, freezing and thawing, and absence of, or inadequate refrigeration. The addition of 50 per cent glucose, or a large amount of 5 per cent glucose at room temperature added to cold blood, such as happens when the intravenous is started with glucose and the blood backs up into the glucose throughout a long operative procedure, may also result in extensive hemolysis, according to De Gowin.[16]

PYROGENIC REACTIONS

The non-specific reactions characterized by chills and fever of varying degree were observed much more frequently associated with the indirect or citrate method of transfusion. In fact, the citrate itself and the so-called precoagulative changes in blood transferred by this method were blamed for these annoying, though rarely serious reactions until Seibert[9, 10] in 1923 showed they were due to certain nonpathogenic bacteria producing thermostable protein substances in the water, now designated as pyrogens.

The great difficulty of freeing contaminated water of these pyrogens in the average hospital solution room has resulted in a new and profitable business, that of manufacturing and distributing pyrogen-free intravenous solutions, which materially increases the cost of medical care.

TRANSFUSION TRANSMISSION OF DISEASE

The transmission of syphilis by transfusion was reported soon after the discovery of the A.B.O. blood types and its resulting re-establishment as a safe therapeutic procedure. Fordyce[18] referred to the case of Dade in 1915 and McClure[7] published his own case report in 1916.

In the 25 years following these first reports over 100 cases of syphilis resulting from transfusion either were reported privately or were published.

This was in the period during which the serologic tests for syphilis were being improved and standardized and before blood banking came into general acceptance and use. Eichenlaub and Stolar[19] state that in 18 out of 41 cases, or 44 per cent of transfusion syphilis, serologic tests would have been of no assistance. Apparently the greatest hazard is with the donor in the preclinical serologically negative stage as McClure's case was.

The present use of supersensitive screen tests for syphilis, such as the Kahn presumptive and the Kline exclusion, will pick up the infection earlier. The storage at 4° C in the refrigerator for a period of three days will kill the treponema pallidum if present. The use of both these precautions should eliminate transfusion syphilis. When friends and relatives are used, it is occasionally difficult to find a donor with a negative serologic test for syphilis. In one case each of seven donors had to be refused on this basis. Hoxworth and Skinner[20, 21] found 7.5 per cent of blood drawn from 3487 donors showed positive precipitation tests and it was discarded on that basis. If 7.5 per cent of the 13,500,000 units of blood collected by the American Red Cross during World War II had been discarded, more than a million units would have been wasted. At the present time serologically positive blood should be sterilized or refrigerated and the plasma used for fractionation.

The transmission of malaria by transfusion is, of course, less serious than the transmission of syphilis. The first case was reported in 1920 by Woolsey,[22] and since that time some 85 cases have been published. Wang and Lee[23] in 3700 transfusions in China found benign Tertian malaria in 14 per cent of their patients. Although benign Tertian malaria is the usual type transmitted, McClure and Lam[24] reported two cases of quartan where the donors were Italians with no symptoms of or exposure to malaria for many years.

Here neither storage in the refrigerator at low temperatures nor examination of blood smears is of material assistance. Exclusion of donors who have had malaria or are from known malaria countries or regions, is apparently the only method of prevention unless some method of actual sterilization is found.

The most serious of all the diseases transmitted by transfusions of blood and plasma is homologous serum jaundice, which was first recognized as a separate entity in 1937. Oliphant[25] reported jaundice following the administration of human serum in 1943. Neefe, Stokes, Reinhold and Lukens[26] in 1944 studied hepatitis due to the injection of homologous blood products in human volunteers, and Paul, Havens, Sabin and Phillip[27] did transmission experiments in serum jaundice and infectious hepatitis in 1945. Grossman, Stewart and Stokes[28] reported post-transfusion hepatitis in battle casualties and its prophylaxis by means of human immune globulin late in 1945. Brightman and Korns[29] found an incidence of 4.5 per cent of homologous serum jaundice from pooled plasma in this country in 1947, a year after Spurling,

Shone and Vaughan[30] reported an incidence of 7.3 per cent among 1054 patients receiving pooled plasma in England.

McGraw, Strumia, and Burns,[31] published in 1949 the results of a four-year survey to determine the incidence of post-transfusion hepatitis as it occurred at the Bryn Mawr Hospital. Of 936 transfused patients there were 32 or 3.5 per cent with probable or possible hepatitis. These patients received 3723 transfusions, hence there was one case of probable hepatitis for every 300 units of blood transfused. Of 528 patients receiving plasma from small pools of eight or ten units with or without whole blood, ten had probable hepatitis, an incidence of one in every 235 plasma transfusions. As pointed out by these authors, the lower incidence of hepatitis in this group is probably due to the small pools of plasma, eight to ten units, as contrasted with pools of 25 to 50 in the American Red Cross material and up to 800 in the British pools.

In the Henry Ford Hospital Steele[32] has studied 26 cases of homologous serum jaundice and 63 cases of infectious hepatitis occurring over a two-year period. Of the 63 cases of infectious hepatitis three died, giving a mortality of 4.8 per cent. Of the 26 cases of homologous serum jaundice nine died giving a mortality of 34 per cent. The mortality of 34 per cent as compared with 4.8 per cent for infectious hepatitis is unusually high. Eighteen of the latter group received their transfusions in the hospital. Three received plasma only, 11 received whole blood alone and four received both blood and plasma. Since approximately 8000 transfusions were administered within the hospital in these two years, there was one case of jaundice for every 440 transfusions.

Case 2.—H. T., Hosp. No. 385096, was a white female, age 18, and married. She was re-admitted to the hospital June 14, 1948, and died June 18, 1948. The patient was a primipara with an uneventful prenatal course. P. E. was negative throughout, essentially. Her Hb. on October 4, 1947, was 11.5 Gm., Rh factor was positive, and blood group O. The delivery was by outlet forceps on April 5, 1948. Left mesiolateral episiotomy was done. Upon delivery of the placenta the patient bled profusely in spite of intravenous pitocin and ergotrate and massage of the uterus. The patient was given 1000 cc. of plasma and this was followed by 1500 cc. of blood group O, Rh positive, donors. Following this the patient's blood pressure improved, and she was returned to her room in fair condition. The patient was discharged from HFH on the seventh postpartum day. T. 99, pulse 108. The Hb. was 12.0 Gm. The patient was seen in the Clinic on May 11. At that time the uterus was forward, undergoing normal involution. Intervening examinations were uneventful. On June 11 she complained of generalized malaise and some pain in her chest. Her lungs were clear. She was urged to have some rest. On June 14, 1948 she was admitted on G. I. service. She had been jaundiced for 3 preceding days, and had had persistent nausea since her delivery and vomiting for the preceding week. Temperature was 101.8°, BP 130/68, and there was a definite icteric tint of the skin and sclerae. The liver was palpable and tender 7 cm. below RCM; otherwise negative. Hb. 12, RBC 4.36, WBC 7150, with 62 per cent PMN, 38 per cent L. Routine urine analysis was negative. Quant. urine urobilinogen .38 units per 100 cc. The prothrombin time was 25″—27 per cent, and

cephalin cholesterol was 4+. The thymol turbidity was 3 units, the Icterus index 82, and the basic phosphatase 7.37.

The patient was given I. V. protein-hydrolysate solution, choline chlorides, vitamin B complex, high protein, high carbohydrate diet. She developed a febrile reaction to protein-hydrolysate and went into a delirium, became semicomatose and developed generalized convulsions. Blood sugar on June 18 was 26 mg. per 100 cc. She died that evening, following a convulsion.

Autopsy showed generalized icterus with 200 cc. yellowish-green fluid in each pleural cavity, 1000 cc. of greenish abdominal fluid, and numerous petechiae over serosal surfaces. The liver was soft, semifluid in consistency, and weighed 950 Gm. The kidneys weighed 200 Gm. each, showing considerable bile staining.

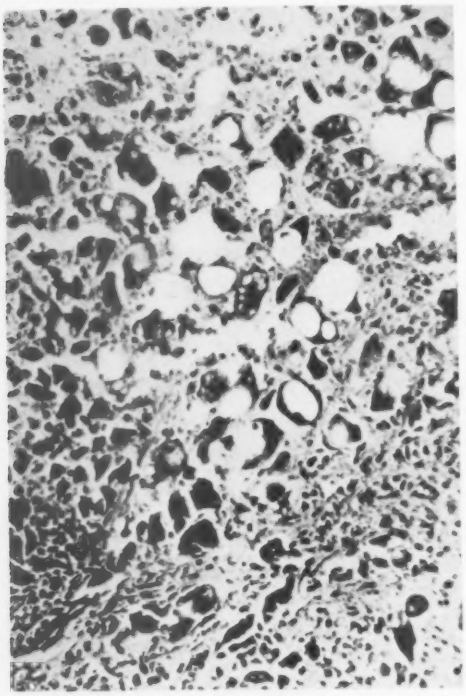

FIG. 2.—Photomicrograph, medium power, showing fatty degeneration and necrosis of liver cells.

The microscopic pathology showed almost complete necrosis of liver cells, leaving only lobular framework, with fine, granular, pink-staining debris scattered throughout.

The anatomical diagnosis was acute necrotic hepatitis (homologous serum jaundice).

CONTROL OF HOMOLOGOUS SERUM JAUNDICE

Since the etiologic agent of homologous serum jaundice has not been isolated and no susceptible animal has been found, the laboratory is of little aid in the diagnosis. This necessitates control measures of the less direct and less adequate type. Careful selection of donors and limitation of plasma pools to one to ten units appears in McGraw, Strumia and Burns' work[31] to be helpful. Stokes, Blanchard, Neefe, Gellis and Wade[33] found that two injections of gamma globulin made from large pools of human plasma given during the incubation period were highly protective in one hospital, while in two other hospitals it was of little value.

Oliphant[25] in his Harvey lecture 1944 stated: "Since jaundice has repeatedly followed the administration of whole blood and blood products, there is an urgent need for some means of detecting the presence of the jaundice producing agent in the blood and for some practical method for treating blood products, so that the danger of jaundice following their use may be eliminated." At the same time he reported that irradiation of pooled serum in a Quartz cell with a mercury vapor lamp for 2½ seconds inactivated the icterogenic agent. Oliphant and Hollaender[34] followed this with a report of the use of irradiated serum in human volunteers in which four out of 12

receiving the control material and one of 12 receiving serum irradiated for six minutes developed jaundice.

This work was followed by numerous applications of the irradiation principle with various types of equipment. MacCallum[35] in England was unable to confirm Oliphant's work,[25] but more recently Habel and Sockrider,[36] Wolf, Mason, Fitzpatrick, Swartz, and Levinson,[37] and Blanchard, Stokes, Hampil, Wade, and Spizizen[38] have confirmed and extended the method and application. The latter group, after trial on human volunteers, find irradiation safe and effective. The treated plasma showed no alteration in the electrophoretic pattern, and they recommend its routine use.

Hartman and Mangun[39] recently demonstrated the feasibility of chemically inactivating viruses in both plasma and whole blood, using methyl-bis (beta-chloroethyl) amine (HN2) and related alkylating compounds. It was shown that these compounds exerted a satisfactory inactivation of five neurotrophic viruses, viz., New Jersey vesicular stomatitis, lymphocytic choriomeningitis, St. Louis encephalitis and Eastern and Western equine encephalitis, in the presence of whole blood and blood plasma. These findings are supported by the observations of Tenbroek and Herriott,[40] and Rose and Gellhorn[41] on the virucidal action of HN2 on five other viruses in the absence of blood.

The method is simple and easily applied. The HN2 or related compound is dissolved in distilled water and added directly to the blood or plasma. The treated material must have a pH above 7.3 to permit rapid degradation of the excess HN2 and below 7.8 to obtain maximum virucidal activity. The treated material is then stored at 4 to 10° C for not less than five days, then a small amount of sodium thiosulfate is added to decompose any remaining traces of HN2. Before use a sensitive color test is applied to further insure that no active toxic agent remains.

EFFECT OF HN ON PLASMA

HN2 is not without certain disadvantages. It partially inactivates components of the clotting system, including prothrombin and accelerator globulin. The amount of fibrin formed is not altered, but the rate at which it forms is appreciably slowed even when preformed thrombin is employed as the clotting agent.

Complement, syphilis antibodies (Kolmer Wassermann), and *B. abortus* antibodies (complement fixation) are only very slightly reduced by sterilizing dosages of HN2.

No significant changes occur in the albumin/globulin ratio nor in the electrophoretic pattern of treated plasma.

The thermal stability of albumin is not significantly altered, according to Mulford,[42] although the reaction of HN2 with albumin has been demonstrated to occur (Mangun[43]).

In the course of the reaction of HN2 with plasma, the formation of toxic intermediary addition products with proteins has been shown to take place.

These further degrade to nontoxic end products, but suitable conditions of pH must exist to ensure their disappearance.

EFFECTS OF HN_2 ON RED BLOOD CELLS

At dosages of HN2 required to sterilize whole blood (500 mg./l), there is a remarkable absence of effects upon the red blood cells. It has been shown by our laboratory that even at dosages of HN2 several times that required to sterilize whole blood, the red blood cells behave in all respects *in vitro* similar to the control specimens. There is virtually no increase in fragility to hypotonic solution. The rate of loss of potassium from the red cell is similar to that of the controls. On long standing, the degree of hemolysis of the treated blood is, if anything, slightly less than in the untreated controls. Sedimentation rate remains essentially normal. Glycolysis, as measured by the disappearance of glucose, is unaffected. Conversion of hemoglobin to methemoglobin on long standing proceeds at about the same rate in treated and untreated blood. The hemoglobin absorption spectrum is unaltered. No studies have been made on the oxygen dissociation constants, nor on the activity of carbonic anhydrase.

The *in vivo* survival of the red blood cells has been investigated both in this laboratory and by F. H. Bethell at Ann Arbor. Both of these investigations have led to a similar conclusion—the *in vivo* survival of the red blood cells is equal to that of the control bloods, if not slightly superior.

GENERAL

The principal disadvantage to the use of HN2 in the sterilization of plasma and whole blood lies in its toxicity. Although it hydrolyzes over a period of hours or days, depending upon temperature and pH, the toxicity of the original compound and some of its intermediaries and intermediate protein addition products requires that careful control be exercised over the process. The greatest single danger lies in the stabilization of the protein addition product by pH values below 7.2. It is, therefore, necessary in the sterilization of whole blood to collect the blood in a modified ACD solution to which alkali has been added, so that the pH of the blood after the addition of HN2 will never be lower than this value. Adequate precautions must then be taken to insure that the blood is not released until the aging period has expired.

Hartman and Mangun[39] have been conducting further studies on new virucidal agents. At least three separate families of compounds have now been discovered which possess a high order of virucidal activity *in vitro* in the presence of plasma or whole blood. While HN2 at the present time is superior to other agents for the treatment of whole blood, there appears to be little doubt that these investigations will eventually disclose other compounds equal or superior to HN2 in their virucidal activity, yet eliminate the dis-

advantages of this particular substance. In the meantime, in view of the urgency of this problem, clinical application of HN_2 on a substantial scale to the sterilization of plasma is being carried out. In a total of approximately 975 plasma transfusions given over a period of ten months to approximately 400 patients, not a single case of hepatitis has been observed in contrast to a predicted 20 cases in untreated plasma.

No evidence of unfavorable reaction nor hematologic changes has occurred in adults or older children. In the course of these studies leukopenia occurred in very young children prior to the recognition of the intermediate protein-HN_2 reaction-product previously mentioned. Since this hazard has been recognized, a color test has been developed to detect this substance and the sterilization procedure modified to eliminate possible danger.

SUMMARY AND CONCLUSIONS

1. The present-day large scale use of blood transfusions keeping pace with the constantly increasing range and extent of surgical procedures is a protection. It involves a correspondingly increased risk, particularly in the way of hemolytic reactions with possible kidney insufficiency and homologous serum jaundice with liver necrosis and insufficiency.

2. To avoid hemolytic reactions greatest care must be exercised in the medical supervision and operation of the blood bank and the whole transfusion procedure. Probably the smoothest and safest operation is obtained by a transfusion team which is responsible for every phase from the original bleeding of the donor, sterilization, grouping, cross agglutination, storage of the blood and the final administration to the patient.

3. To eliminate homologous serum jaundice, nothing short of sterilization of both plasma and whole blood seems acceptable.

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DISCUSSION.—DR. EVERETT I. EVANS, Richmond, Va.: I think some of us who are not too well acquainted with the theoretical and practical import of this paper may not recognize its true significance. One reason is that, as surgeons, we tend more and more to delegate the care of patients to people who are not directly responsible for the fatality that may ensue. In my experience and the experience of Doctor Bigger in our hospital, and I think in the experience of most people who are interested in the matter of replacing material lost from the blood stream through trauma or surgical operation, it becomes evident at once that what is needed in replacement therapy is not plasma, but whole blood. I have said that so often that I am beginning to be ashamed of saying it again; but it must be understood. We need blood, not plasma. If that is understood there need not be much plasma made, and if that dictum is followed there will not be anywhere near the danger of transmission of serum hepatitis. The great hazard of transmission of hepatitis virus by plasma as contrasted with whole blood results from the *pooling* of plasma. This greater hazard is a simple mathematical matter. So I say again that we should impose on ourselves the idea that we need whole blood, not plasma, and thus we will greatly lessen the incidence of serum hepatitis.

I believe more work should be done on preparation and trial of so-called plasma substitutes, until we have methods that will truly sterilize plasma; to date this has not been done. We are extremely interested in the work Doctor McClure's group is doing with Doctor Hartman in the use of nitrogen mustard, but a vastly greater trial of this material must be carried out before we can be sure it is safe.

Finally, I will only say again that in the problem of replacement therapy, whole blood is the agent that is needed, and not plasma.

DR. ALLEN O. WHIPPLE, New York: Doctor McClure asked me to say a few words about the use of transfusion, possibly because they have more transfusions at Memorial Hospital than in any other hospital in the city of New York. There is no question that transfusion is one of the greatest aids to the surgeon, and yet the amount of blood to be

given at the time of operation, and often the rapidity with which it is given, is left to someone who is not so completely involved in the technic of the operative procedure—the anesthetist, as a rule, is the one who informs the surgeon of the need for more blood. The fact that patients pick up so rapidly with transfusion, and frequently with multiple transfusions during an operative procedure, has a tendency to increase the use of transfusions, and yet I am sure that patients not infrequently are given too much blood.

There are a number of interesting problems aside from this important one Doctor McClure has discussed, namely, the use of nitrogen mustard. We do not know what becomes of these millions of foreign bodies that we are putting into patients. We are sure they are compatible and all that, but they are foreign bodies, and I am sure that in the future more work will be done in studying what happens to these foreign red cells that are put into patients. Another interesting phenomenon which we are observing at the Memorial Hospital is the fact that many of the patients who get a great deal of blood later develop the syndrome of metabolic alkalosis or potassium deficiency. One would think that with all the red cells that are being put into these patients the potassium coming from these red cells, if they are not altogether compatible, would make up for some of this potassium deficiency. Some of the most marked examples of potassium deficiency have occurred in patients who have had multiple transfusions, and it would seem that the field for further study of transfusions is a vast one. Doctor McClure and his group have started an investigation which is extremely important and we have watched it with great interest. I certainly congratulate him on the presentation of this very important paper.

DR. ROY D. McCLURE, Detroit (closing): It is known that many blood banks have thrown away a great deal of the stored plasma because of the serious complications resulting from its use, in infecting patients with either infectious hepatitis or homologous serum jaundice. Of course, the infection can come by the use of whole blood if that is taken from a donor harboring either of these viruses. The danger is much less when a single blood is used, as one person can infect the pooled plasma or serum of anywhere from two to 100 persons in the bank if that many are pooled.

One factor that has led to slow development of this knowledge, and it is a factor which has protected both physician and hospital perhaps from lawsuits (such suits have been filed) is that the incubation period of homologous serum jaundice varies from 60 to 90 days. The patients have left the hospital and, as they develop jaundice three months later, do not associate it with the hospital stay. We do advocate at this time chemical sterilization of plasma and smaller pools of plasma.

Doctor Hartman and Doctor Mangun are working in our laboratory with other chemical sterilization agents, dimethyl-sulphate and diacetyl-ethylene, which appear to have even greater promise. The chemical formula for HN_2 is $CH_3N(CH_2CH_2Cl)_2HCl$.

Doctor Whipple mentioned a potassium deficiency with transfusions. This is mentioned in the body of the paper which I did not have time to give today. I thank Doctor Whipple and Doctor Evans for their discussion.

SICKLE CELL ANEMIA: A SURGICAL PROBLEM*

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THE DRAMATIC CLINICAL PICTURE presented by the patient with sickle cell anemia has in numerous instances led to unnecessary operation. The literature contains several reports by internists and clinical pathologists of errors in surgical diagnosis, many of which have resulted in unnecessary operation in patients with sickle cell anemia.[1-4] Relatively little has appeared in the surgical literature on the subject. However, in 1935 Campbell gave an excellent report on abdominal pain in patients having this disease.[5] Canby reported a case in 1944 in which a preoperative diagnosis of torsion of the spleen or volvulus of the small intestine was made. Laparotomy revealed multiple infarcts of the spleen resulting from sickle cell anemia.[6] Bauer has suggested that all Negro patients should be tested routinely for sicklemia to obviate these errors in diagnosis.[7] The purpose of this paper is to call to the attention of surgeons the importance of a knowledge of sickle cell anemia in the diagnosis of the numerous and varied symptoms which may be experienced by patients having this disease.

ESSENTIAL FEATURES OF SICKLE CELL ANEMIA

Approximately 10 per cent of Negroes possess an inherited anomaly which is characterized by a change in shape of the erythrocytes from spherical and discoid forms to bizarre multipointed forms when the red cells are placed in an environment of reduced oxygen content. Individuals whose red cells undergo "sickling" are said to have the sickle cell trait or sicklemia. The majority have no physical abnormalities or symptoms referable to the inherited anomaly, although it has been claimed by some that patients with sicklemia are bad operative risks and that their life expectancy is reduced. A small number of individuals estimated as one in 40 with demonstrable sickled cells develop sickle cell anemia.

Sickle cell anemia is a chronic disease, usually becoming manifest in infancy and continuing thereafter, but varying in severity and age of onset. There is evidence of increased red cell destruction, jaundice of a hemolytic type, and evidence of increased red cell regeneration as revealed by hyperplastic bone marrow, osteoporosis of cancellous bones, nucleated red cells in the peripheral blood, and an increased number of recticulocytes.[8-11] Recurrent febrile episodes occur in which the patient has severe pains and has to stop work or play. Patients examined during one of these so-called "crises" are obviously

* Read before the Southern Surgical Association, Hot Springs, Virginia, December 6, 1949.

quite sick, often writhing with pain, have a septic type of temperature, and a high leukocyte count. The disease in its varied manifestations simulates many surgical conditions, a list of which is given in Table I.

At autopsy the most common findings are congestion of smaller blood vessels with sickled erythrocytes, thrombosis, infarction necrosis, and replacement of the parenchyma by scar tissue.[12] All organs of the body may be involved, but the viscera most commonly involved are the spleen, bones, and central nervous system.[13] Less commonly involved are the kidney, liver, skin, and intestinal tract.

One of the explanations given for the observed pathologic changes is that red cells sickle in the body and that the blood containing sickled cells in large numbers is more viscid and circulates less readily. Any condition which favors mechanical stasis or which causes an increase in plasma viscosity favors stasis of blood. Stasis in turn causes anoxia, anoxia causes

TABLE I.—*Surgical Features of Sickle Cell Anemia.*

1. Acute abdominal symptoms	4. Leg ulcers
2. Jaundice	5. Priapism
3. Bone and joint pains and deformity	6. Hematuria
	7. Cerebral accidents

sickling, sickling causes increased viscosity, which in turn favors stasis, thus a vicious cycle occurs. The result of this process is injury or necrosis of tissue with its attendant symptoms and signs depending on the location and the blood vessels involved.

The increased number of leukocytes and nucleated red cells and platelets and the anemia *per se* are additional factors favoring stasis and anoxia. Occasionally in sickle cell anemia, as emphasized by Kimmelsteil, there is a patchy and massive ischemic necrosis without demonstrable thrombosis, which brings up the possibility of vasoconstrictor factors.[14] Whatever the final facts are concerning the explanation of this disease, sickle cell anemia is characterized by alterations in blood which lead to the production of clinical syndromes that are of interest to the surgeon.

FEATURES OF SURGICAL INTEREST IN SICKLE CELL ANEMIA

The surgeon's interest in this disease is most likely to be aroused because of varied abdominal symptoms and signs which may be found in patients with sickle cell anemia.[15-19] The acute abdominal pain experienced at times by these individuals may strongly suggest the possibility of intussusception, intestinal obstruction, acute appendicitis, ureteral colic, or perforation of a hollow viscus. Fever, leukocytosis, and increased jaundice of a variable degree are frequently present during acute exacerbations of the disease. Since gallstones are common in such individuals the question of acute cholecystitis may be raised when a patient complains of severe right upper quadrant pain

which is accompanied by jaundice, fever, and leukocytosis.[20] The bone and joint pain of these patients on several occasions has been confused with that of acute rheumatic fever.[21-23] In certain instances severe localized bone pain may be of such a degree as to suggest the presence of acute osteomyelitis.[4, 24, 25] In some individuals striking bone changes are found by roentgen examination. A coarseness of architectural pattern may be present in the bones. In some instances striking changes have been noted in the skull, and aseptic necrosis, followed by collapse of the femoral head, has been observed.[26, 27]

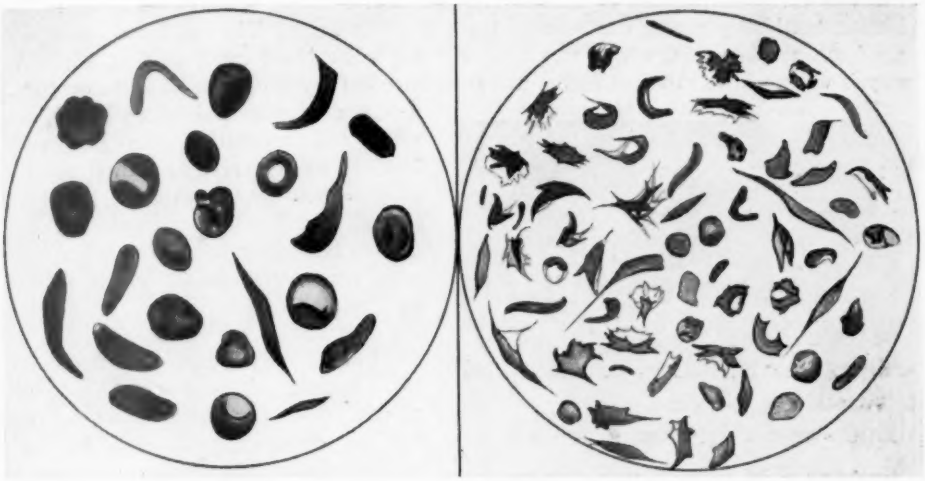


FIG. 1 FIG. 2

FIG. 1.—Sickle cell morphology as seen in smear stained by Wright's method or in a fixed tissue preparation.

FIG. 2.—Sickle cell morphology as seen in moist preparation after the cover slip has been sealed with petroleum jelly for a few hours.

Leg ulcers are more prone to occur in adults than in children. The ulcers present a difficult problem in management and may recur after what appeared to be a cure resulting from skin grafting.

Of especial interest to the urologist is the fact that priapism may be present for a period of days and may be quite resistant to management.[28-30] Also of practical importance to the urologist is the fact that hematuria may occur, and when associated with pain in the flank may present the picture of renal colic.[31]

The preceding paragraphs have stressed the fact that sickle cell anemia may present symptoms and signs which resemble a variety of acute intra-abdominal lesions. It is equally important for the surgeon to remember that patients with sickle cell anemia are just as prone to have acute abdominal conditions as are members of the general population. The following case reports are given to illustrate some of the surgical problems mentioned above.

CASE REPORTS

Case 1.—Diagnosis was intussusception, laparotomy was performed with negative findings, and sickle cell anemia was subsequently proved.

R. B., No. 48557, colored female, age 7 months, was admitted to the surgical service on April 24, 1943, because of colic and bloody stools. Approximately 6 hours before admission she appeared to be having episodes of abdominal pain. Two loose stools were passed following the onset of pain, the last stool containing a small amount of blood. There had been no vomiting. The past history was noncontributory.

The temperature was 99° F., the pulse rate 110, and the respirations 20. The patient was well nourished and well developed and was apparently having pain. The abdomen was soft and not distended. Tenderness on palpation was not significant. A 3 cm. mass was thought to be palpated in the left mid-abdomen. Nothing was felt on rectal examination, but bloody mucus was seen on the examining finger. The red blood count was 3,300,000, the hemoglobin was 10.5 Gm., and the white blood count was 15,200. Urinalysis was negative. Barium enema was suggestive but not diagnostic of intussusception.

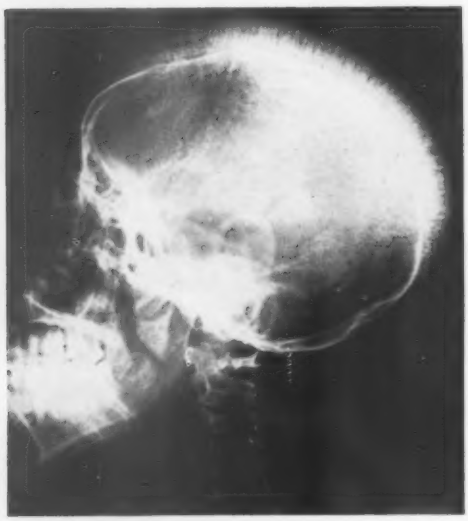


FIG. 3.—Roentgen ray film of skull of patient with sickle cell anemia showing perpendicular "hair on end" trabeculations of new bone.

A diagnosis of intussusception was made and laparotomy was performed. Nothing was observed to suggest that intussusception was present or had been present. Sickle cell anemia was diagnosed on two subsequent admissions when joint pains were present in addition to abdominal pain.

Case 2.—Symptoms were suggestive of intestinal obstruction. Sickle cell anemia was considered preoperatively and the diagnosis established. Findings made exploration appear necessary. Negative findings were obtained on exploration.

T. S., No. 11749, a 5-year-old colored boy, was admitted to the pediatric service on January 12, 1939, with an admission diagnosis of "possible intestinal obstruction." He was complaining of severe upper abdominal pain of eight hours duration without any localization. There was no vomiting. He was severely constipated and no bowel movement had resulted from the use of either magnesium sulphate or enemas.

On examination the temperature was 100° F. and the pulse rate 120. He appeared very fretful and acutely ill, preferring to lie on his side with his legs drawn up on his abdomen. Abdominal distention and generalized tenderness were present with considerable rigidity which was thought to be partially voluntary. No masses were palpable and the abdomen was silent on auscultation. The rectal examination was negative. On admission the red blood count was 1,470,000. White blood count was 17,150 with 77 per cent granulocytes and the hemoglobin was 5.8 Gm. Urinalysis was negative. Roentgenograms of the abdomen showed some gaseous distention of the small bowel and proximal colon.

Sickle cell anemia was suspected because of evidence of anemia in combination with the above complaints. The diagnosis was confirmed when moist preparations revealed immediate sickling of the red blood cells. However, abdominal signs were so marked

emergency surgical consultation was obtained. A diagnosis of acute surgical abdomen was made and laparotomy was performed. There was no evidence of an intra-abdominal lesion.

Case 3.—Pain, fever, leukocytosis, and jaundice were present, with a history of healed leg ulcers. A diagnosis was made of acute appendicitis. An acutely inflamed appendix removed. Patient also proved to have sickle cell anemia.

L. M., No. 1666, Vol. 113, colored female, age 20, was admitted to the surgical service on February 13, 1938, with an admission diagnosis of acute appendicitis. She was complaining of pain in the right lower quadrant of her abdomen with associated nausea and vomiting of 20 hours duration. Her past history revealed episodes of joint pains with jaundice and leg ulcers.

The admission temperature was 100.6° F. and the pulse rate was 96. Examination revealed a very thin, anemic appearing young female. The sclerae were jaundiced. The heart was enlarged, with a loud systolic murmur heard over the precordium. There was marked tenderness in the right lower quadrant of the abdomen, with rebound tenderness in the right lower quadrant of the abdomen, with rebound tenderness and muscle rigidity. There was a healed ulcer on the medial side of the right ankle. The red blood count was 1,770,000, the hemoglobin was 6.6 Gm., and the white blood count was 21,000 with 87 per cent granulocytes. The urinalysis revealed specific gravity of 1.010, albumin 2 plus, sugar negative, acetone 1 plus. Microscopic examination was negative.

A diagnosis of acute appendicitis was made and appendectomy performed. An acutely inflamed appendix was found and removed. Moist preparations of blood later confirmed the diagnosis of sickle cell anemia.

Case 4.—History of trauma of the abdomen was obtained. Severe abdominal pain was present, with tenderness on abdominal and rectal examination. The atypical character of the pain and the presence of joint complaints raised question of sickle cell anemia, which was verified by a moist smear. No operation was performed.

A. W., No. 139205, a 20-year-old colored boy, was admitted to the surgical service on October 17, 1948, because of severe abdominal pain. He first noticed this pain 12 hours prior to admission when he "came to" in an empty lot after a drunk, during which he thought he had been beat up. He was complaining of continuous, severe pain in the right side of his abdomen as well as pain in his lower back and knee joints.

On examination the temperature was 98° F., the pulse rate 82, the respirations 32, and the blood pressure 70 systolic and 40 diastolic. The patient was fairly well developed and well nourished and obviously in severe pain. There was tenderness to pressure over the right side of his abdomen with rebound tenderness and protective rigidity in that region also. No masses were palpable. Auscultation revealed peristalsis which was not considered hyperactive. There was tenderness to pressure on the pelvic floor on rectal examination. The remainder of the physical examination was negative except for pain on passive motion of the knee joints.

On admission the red blood count was 3,780,000, the hemoglobin was 11 Gm., and the white blood count was 5450 with 69 per cent granulocytes. Urinalysis showed a specific gravity of 1.018, albumin 2 plus, and no sugar; microscopic examination revealed an occasional red blood cell and an occasional granular cast.

No definite diagnosis could be made from a roentgenogram of the abdomen. Scattered air throughout the abdomen was suspected to be extrinsic to the bowel suggesting a ruptured viscus. Enlargement of the spleen was noted which was not found on physical examination.

The admission diagnosis was "acute surgical abdomen" from suspected trauma. The associated joint and back pains seen on further observation and the complete absence of external evidence of trauma suggested the possibility of sickle cell anemia. Moist prep-

arations subsequently revealed sickled cells and the patient was later transferred to the medical service.

Case 5.—This was a child referred to surgical service with tentative diagnosis of intestinal obstruction. Previously he had had an appendectomy. The white blood count was 18,550. Surgeon's impression: abdominal pain secondary to sickle cell anemia. A moist preparation established sickle cell anemia. The symptoms subsided.

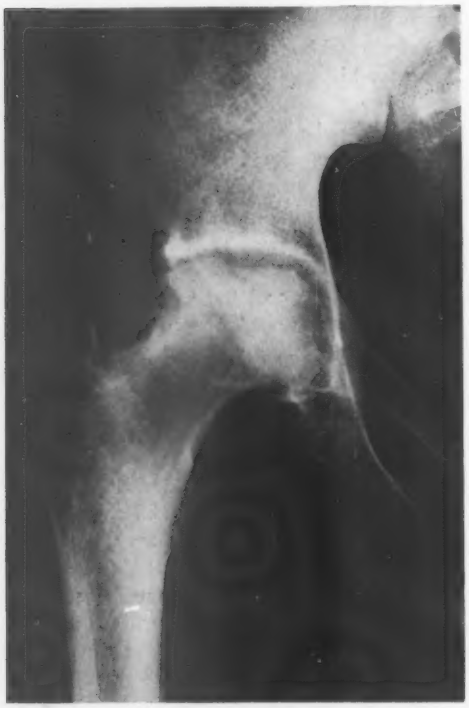


FIG. 4. — Aseptic necrosis of head of femur occurring in a patient having sickle cell anemia without any history of dislocation or other trauma to the hip.

M. P., No. 6321, an 11-year-old colored boy, was admitted to the pediatric service on May 12, 1940, because of abdominal pain of 3 hours' duration. The pain was intermittent in character, very severe, and periumbilical in location. There was no nausea or vomiting. He had passed no gas since the onset of pain. For the previous two years he had been "sickly" and had complained at times of joint pains and aching extremities. Appendectomy had been performed at the age of 3.

On examination the temperature was 98° F., pulse 110, and respirations 20. The patient was apparently experiencing intermittent episodes of abdominal cramping, during which he would cry out because of pain. The abdomen was distended, tense, and tympanitic. Peristalsis was hyperactive. There was some voluntary resistance of the abdominal wall but no rigidity. No tenderness and no masses were demonstrated. The rectal examination was negative.

On admission the red blood cell count was 2,650,000. The white blood cell count was 18,850 with 97 per cent granulocytes, and the hemoglobin was 8.8 Gm. and sickled nucleated red blood cells were seen on the smear. The urinalysis was negative. Roentgenograms of the abdomen in the supine and upright positions did not suggest any specific diagnosis.

A clinical diagnosis of intestinal obstruction was considered, even though the evidence of sickle cell anemia was present, and surgical consultation was requested. The surgical consultant considered sickle cell crisis the etiology of his pain because of absence of vomiting and lack of roentgen ray evidence of obstruction, plus the findings of sickle cell anemia. Rapid improvement followed symptomatic therapy and the patient was discharged to the Pediatric Outpatient Clinic for continual observation.

Case 6.—This patient suffered severe pain in left costo-vertebral angle. Clinical impression: ureteral lithiasis. Roentgen ray showed no evidence of calculi in urinary tract but bone architecture caused the roentgenologist to suggest possibility of sickle cell anemia. Moist preparations confirmed the diagnosis.

S. M., No. 113219, a 23-year-old colored man, was admitted to the surgical service on March 20, 1947. He was complaining of pain in his lower back and abdomen, which

subsequently localized to the left costovertebral angle. The onset of pain was associated with nausea and vomiting. There was no disturbance of urinary or bowel function.

On examination the temperature was 100° F., the pulse rate 86, the respirations 24, and the blood pressure 122 systolic and 70 diastolic. The patient appeared much younger than his stated age and was in no acute distress. There was enlargement of the heart with a systolic murmur present over the precordium. The abdomen did not show any abnormal signs on examination but there was tenderness to pressure in the left costovertebral angle. The rectal examination was negative.

The laboratory examination revealed the red blood count to be 3,310,000, the white blood cell count to be 11,800 with 55 per cent granulocytes, and the hemoglobin 8.5 Gm. The urinalysis showed a specific gravity of 1.013, a pH of 6.5, albumin 1 plus, and no sugar.

A diagnosis of ureteral calculus was considered. Roentgenograms did not show any calcification in the urinary tract but showed bone changes sufficient to suggest sickle cell anemia as a diagnosis. This was substantiated by moist preparations which showed immediate sickling. The patient was discharged asymptomatic to the medical outpatient department after several days observation.

Case 7.—This patient has severe pain and nausea associated with frequency and gross hematuria. She was known to have sickle cell anemia. Diagnosis after urologic study was renal infarct secondary to sickle cell anemia.

T. H., No. 150497, colored female, age 22, was admitted to the urologic service with diagnosis of gross hematuria due to possible cystitis, renal tuberculosis, nephrolithiasis, or acute pyelonephritis. She was complaining of pain in the right costovertebral angle of one week's duration. The pain became very severe 48 hours before admission, at which time gross hematuria occurred. There was some frequency but no dysuria. Headaches, nausea, and general malaise were present since the onset. Her past history included leg ulcers and a known diagnosis of sickle cell anemia.

The admission temperature was 105°, the pulse rate 90, and blood pressure 110 systolic and 70 diastolic. Examination revealed an acutely ill, slender young colored girl in moderate pain. There was marked tenderness over the right upper quadrant and right costo-vertebral angle. No mass was palpable. There were multiple scars from old leg ulcers over both lower extremities.

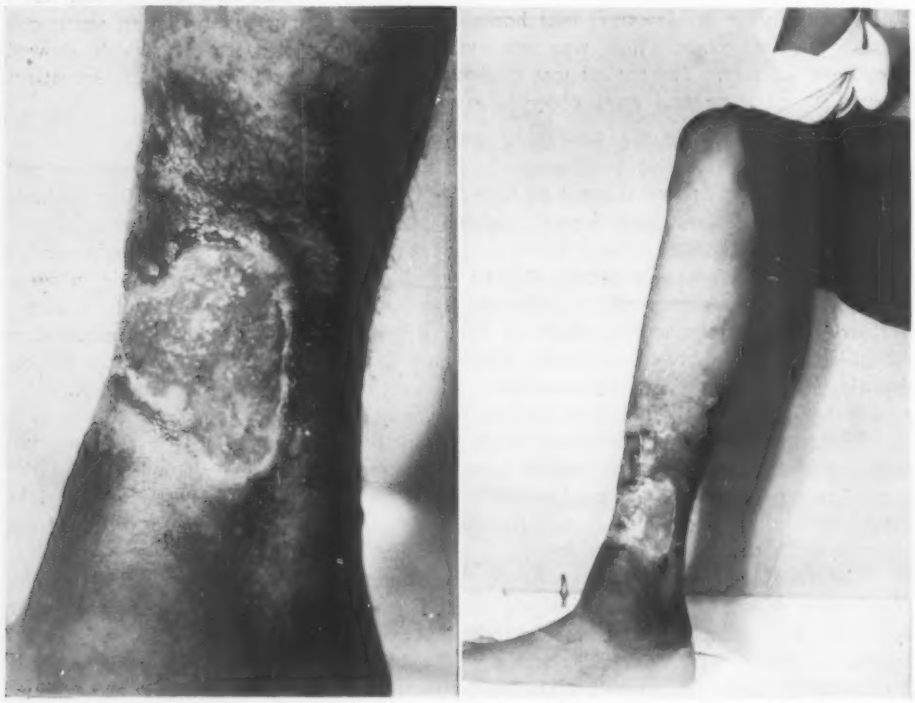
The red blood count was 2,400,000, the hemoglobin was 7.0 Gm. and the white blood count was 27,400. The urinalysis showed gross blood, albumin 3 plus, and sugar negative. Following excretory and retrograde pyelograms a diagnosis of right renal infarct secondary to sickle cell anemia was made. Moist preparation confirmed the diagnosis of sickle cell anemia. The response to symptomatic treatment was prompt and the patient was discharged to the Outpatient Clinic on July 16, 1949.

Case 8.—This patient had chronic leg ulcers, extremely resistant to treatment in a patient known to have sickle cell anemia. He was studied during 21 different hospital admissions.

P. M., No. 17524, colored male, age 31, was admitted to the hospital for the first time on February 22, 1933. His major complaint at this time was leg ulcers of 2 years duration. A diagnosis of sickle cell anemia was made on this admission. He has subsequently spent 1558 days in the hospital during a total of 21 hospital admissions. The predominant complaint has been leg ulcers, but episodes of joint pain, chest pain, abdominal pain, flank pain with hematuria, and jaundice have occurred. In spite of repeated transfusions his blood count has rarely reached 3,000,000. The hemoglobin has seldom been over 8.5 Gm. All attempts to cure the ulcerations have met with failure. Ointments, bed rest, pressure dressings, excision with skin graft, and sympathectomy have been tried. Temporary healing of the ulcers has resulted after long

periods of hospitalization only to be followed repeatedly by a recurrence of the ulceration in a relatively brief period of time.

At the time of his most recent admission on August 24, 1949, his temperature was 99.2° and pulse rate 80. Examination revealed a thin anemic young man with long, slender extremities who seemed much younger than his stated age. The liver and spleen were not palpable. The skin of both lower extremities appeared thin and atrophic. The anterior surfaces of both lower legs were covered with scars and skin grafts. In the region of the medial and lateral malleoli of both legs were large secondarily infected ulcers measuring approximately 3 inches in diameter. There was some improvement on discharge two and one-half months later following bed rest, wet dressings, pressure dressings, and repeated transfusions.



A B

FIG. 5.—Chronic leg ulcer occurring in 19-year-old Negro patient with sickle cell anemia.

SUMMARY AND CONCLUSIONS

1. Patients suffering from an acute attack of sickle cell anemia often present symptoms which may suggest the presence of any of several different surgical lesions.

2. The essential pathologic features of sickle cell anemia are reviewed and the essential features of interest and importance to the surgeon are summarized.

3. Eight illustrative cases are presented.

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DISCUSSION.—DR. R. M. POOL, Memphis: Doctor Wilson's paper is so complete and so accurate so far as the pathology is concerned that it leaves little to be said.

Recently, Doctor Wilson and I saw a Negro in his late sixties who had been admitted to John Gaston Hospital in Memphis because of abdominal pain, nausea and vomiting, as well as other evidence of intestinal obstruction. Roentgen ray examination of the abdomen was also suggestive of obstruction. Sickle cells were found in the blood, however, and for this reason we debated as to whether or not an exploration for obstruction should be carried out. Although the case was questionable, Doctor Wilson and I agreed that the operation should be performed.

On exploration, no obstruction was found. This illustrates exactly the problem Doctor Wilson has presented. On the other hand, we should not forget that people who have sickle cell anemia may also have acute abdominal conditions which demand surgery.

I congratulate Doctor Wilson upon his excellent presentation.

DR. F. E. KREDEL, Charleston, S. C.: Doctor Wilson asked me to say a word on this subject because of the similarity of the Negro population in the hospitals of Memphis and Charleston. We recognize of course a few cases of acute abdominal pain probably due to sickle cell anemia. Rather recently we had a case of an 8-year-old Negro girl with a typical cerebral thrombosis and hemiplegia, which we believed to be caused by sickle cell anemia, who showed very satisfactory response following stellate sympathetic blocks. It seems likely from our knowledge of this condition that the blood probably sludges for quite a while first, before it goes on to a fixed thrombus. For this reason it would seem, in certain parts of the body at least, that an effort should be made to prevent the ultimate thrombosis. The only condition, *in vitro* at least, that seems to prevent sludging and increased viscosity is prevention of anoxia. If you bubble Co_2 or nitrogen through even washed cells in this condition there is a tremendous increase in viscosity. So it seems that in the patient every effort should be made to prevent hypoxia in the acute crises.

DR. WILLIAM F. MACFEE, New York: Since, as you probably know, New York has become one of the largest centers of Negro population in the country, this presentation by Doctor Wilson was of particular interest to me. Just before I left New York to come to this meeting we had in the ward at St. Luke's Hospital in New York a young Negro who was on the medical service and who, like some of the cases described, developed symptoms of an acute intra-abdominal condition. The symptoms were not quite typical of any of the usual things, but suggested acute cholecystitis. At the request of the medical service he was transferred to surgery. Fortunately, the resident staff took the trouble to look up the symptoms of sickle cell anemia and we were spared the chagrin of operating upon this patient.

DR. ELDRIDGE CAMPBELL, Albany, N. Y.: I simply want to add my word of admiration to those of the preceding speakers on the work done by Doctor Wilson and his associates; and to say that even though one has become a neurosurgeon and moved to the North, it does not mean that one does not encounter these curious complications of sickle cell anemia. In the last few years at the Albany Hospital we have seen one individual with a so-called acute abdomen eventually attributed to sickle cell anemia, two who had had cerebral thromboses, explainable only on those grounds; one with back pains and two with what was supposed to have been acute osteomyelitis and never proved. It is particularly noteworthy that acute abdominal pains may occur in individ-

uals who are not in the acute phase of anemia. I know of no single laboratory test that will prove that this is due to sickle cell anemia or to some more obvious cause. The only thing one can do is to bear in mind the possibility of sickle cell anemia in Negroes who have such pain.

DR. HARWELL WILSON, Memphis (closing): I wish to express my appreciation for the discussion by Doctor Pool, Doctor Kredel, Doctor MacFee, and Doctor Campbell. I think Doctor Kredel raised some interesting questions with reference to therapy in these patients. I said nothing about therapy because this study has been concerned primarily with an analysis of symptoms occurring in patients with sickle cell anemia and with the pathologic changes which produce the symptoms and signs mentioned. We hope to be able to report at a later time regarding studies concerned with therapy in these patients.

NEWER CONCEPTS OF BLOOD COAGULATION, WITH PARTICULAR REFERENCE TO POSTOPERATIVE THROMBOSIS*

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WITHIN THE PAST DECADE there has been an increasing interest in venous thrombosis, probably because it has been the consensus of most surgeons that with the control and prevention of two of the principal causes of death postoperatively, shock and infection, the complications following venous thrombosis have become relatively more important. Unquestionably, as the result of better preparation of patients before the performance of an operation of considerable magnitude, the detection and correction of blood volume deficiencies and the replacement of blood loss during operations has been responsible for the almost complete disappearance of shock in the operating room and in the postoperative period. Also the availability of antibiotics and their use has almost completely prevented the development of infection. Although thrombo-embolism has in this way become relatively more important because of the control and prevention of the two other great killers occurring postoperatively, its significance is even of more importance because, as we[1] have shown and has been shown elsewhere, the incidence of thrombo-embolism and death from pulmonary embolism has actually increased in spite of the measures which have been instituted to prevent it.

We have been interested for a number of years in venous thrombosis and have held the opinion that usually it could be prevented, particularly if the precipitating factor responsible for the formation of a clot in the normal vein could be overcome.[2-5] The two factors which are important in the development of phlebothrombosis are (1) a predisposing factor, which consists of increased coagulability of the blood and which occurs in individuals who have been subjected to tissue trauma, and (2) a precipitating factor, which consists of circulatory stasis. It is of little significance whether injury to tissue results from accidental trauma, or by trauma from a neoplastic disease. Whatever the cause, tissue damage results in changes in the blood which increases its coagulability. These changes are the principal or predisposing factors. The precipitating factor in phlebothrombosis, which probably never occurs without slowing of the blood stream, is responsible for the location of the thrombus; with few exceptions the thrombi occur in those veins in which the circulatory flow is likely to be retarded, *i.e.*, the deep veins of the lower extremity.

* Read before the Southern Surgical Association, Hot Springs, Virginia, December 6, 1949.

Aside from diminishing the degree of trauma to which a patient is subjected during an operative procedure by employing as atraumatic technic as possible, there has been little that could be done to prevent the increased coagulability of the blood in these patients. However, it is possible that if all patients subjected to trauma were given anticoagulants many thromboses could be prevented. On the other hand, the routine administration of anticoagulants is far too dangerous because of the possible resultant hemorrhagic tendency. Because of the previous inability to prevent the increased clotting tendency of the blood following tissue trauma, efforts were made to prevent circulatory stasis in the hope that phlebothrombosis could be prevented. Active mobilization of the lower extremities and early ambulation of the patient were practised. Compression bandages were applied to the lower extremities from the toes to the groin, since it was believed that by compressing the superficial veins the blood is shunted into the deep venous system with increased blood flow. Deep breathing was encouraged in order to increase the negative pressure within the thorax to facilitate the return of the venous blood to the heart. Heat was applied to the extremities and to the abdomen to produce vasodilatation of the arterioles in order to increase the vis a tergo in the venous system and to increase the blood flow. In spite of all of these measures which were used to prevent the precipitation of a clot within a normal vein, phlebothrombosis developed frequently.

It was further thought that even though venous thrombosis did occur in spite of prophylactic measures used, prompt recognition of phlebothrombosis and the introduction of therapeutic measures would prevent the detachment of the clot and a fatal pulmonary embolism. Constant vigilance of all patients who were bed-ridden and who were likely candidates for the development of venous thrombosis was maintained. The lower extremities were carefully examined twice daily, and although a fairly large number of phlebothromboses were discovered, there were unfortunately a number of patients with negative findings who developed pulmonary embolism, some of whom died.

In a study over a seven-year period, ending June 30, 1948, of the cases of venous thrombosis at the Charity Hospital in New Orleans, we[1] found that there was an actual increase in the incidence of thrombo-embolism, both of the fatal and non-fatal varieties. Of all the cases of thrombo-embolism, and this includes not only cases of phlebothrombosis but also the cases of thrombophlebitis, the number per hundred thousand admissions seen at the Charity Hospital in the five-year period from 1941 to 1946 was 147, whereas in the later two-year period, 1946 to 1948, the number increased to 230. The number of cases of embolism per 100,000 admissions in the respective periods were 51 and 139 and the number of fatal pulmonary embolisms in the respective periods were 45 and 95. It is thus seen that in spite of measures which have been taken in an institution where considerable emphasis has been placed upon the prevention and treatment of thrombo-embolism, not only has the incidence increased, but the cases of non-fatal and fatal pulmonary embolism have increased. The figures suggest that there was not the proportionate

increase in the number of cases of fatal pulmonary embolism as there was in the cases of non-fatal pulmonary embolism, which is probably due to the fact that many of the patients who had potentially fatal pulmonary emboli were saved by the ligation of their veins.

In the seven-year period there were 580 cases of thrombo-embolism, 316 of which were uncomplicated by embolization, and 264 associated with pulmonary infarction or embolism. It is difficult to say what is responsible for this increase in the incidence of thrombo-embolism, which has increased in spite of everything that has been done to prevent it. That this is not unique in the Charity Hospital is evidenced by the results obtained at the Massachusetts General Hospital.

In a recent report based on autopsy series by Roe and Goldthwait[6] there was a progressive increase in the incidence of pulmonary emboli. The cases were divided into three periods: 1931 to 1935; 1936 to 1940; and 1943 to 1947. The respective percentages of pulmonary emboli in the autopsy cases were 2.16 per cent; 3.66 per cent and 4.42 per cent. This increase is significant, because from 1943 to 1947 the number of both therapeutic and prophylactic femoral vein ligations has progressively increased. Dr. Clayton Jones,[7] Assistant Editor of The Lancet, states that the death rate in England from hemorrhagic infarction of the lung has increased. "This includes embolic pneumonia, infarction of the lung and pulmonary thrombosis, as well as pulmonary embolism, and it would not include cases where the certifying doctor indicated that the condition was a combination of surgery, because these are coded under the condition for which the operation was done. The deaths under this heading were fairly steady at 168 to 268 yearly between 1931 and 1943, but thereafter the numbers have risen: 1944, 297; 1945, 266; 1946, 381; 1947, 438; and 1948, 462."

Whether the increase in the incidence of thrombo-embolism is due, as we[1] previously suggested, to the increased coagulability of the blood resulting from the almost universal use of antibiotics in hospitalized cases or whether it is due to the administration of large amounts of blood in preparing patients for operation which in itself might increase the coagulability of the blood, one cannot say. There is some evidence to show that antibiotics do increase the blood coagulability. Moldavsky, Hasselbrook, and Cateno[8] demonstrated that patients receiving penicillin injections exhibited an increased coagulability of their blood. This work was corroborated by Macht.[9] More recently Macht and Farkas[10] demonstrated that aureomycin, when administered to patients and to animals, caused a definite shortening of the blood coagulation time. On the other hand Dolkart *et al.*[11] found that the administration of penicillin in oil and wax caused no change in the clotting time, prothrombin time or heparin tolerance curve. Similar negative results were obtained when penicillin G was administered in saline solution. These results have been corroborated by Weiner[12] and Lewis.[13] The fact that the incidence of thrombo-embolism on the medical services was almost as high as it was on the surgical services would suggest that the administration of blood had little or nothing

to do with the development of venous thrombosis, since relatively few of the patients on the medical services receive blood transfusions whereas a good many of the patients on the surgical services received large amounts of blood.

With the exception of the obstetric, gynecologic, and tuberculosis services there was a distinct parallelism between the number of admissions to the service and the number of cases of thrombo-embolism. Whereas 20.2 per cent of the admissions were on the obstetrical service, only 9.8 per cent had thrombo-embolism; 8.7 per cent of the cases were admitted to the gynecologic service, and 18.1 per cent had thrombo-embolism. This difference may be more apparent than real, because septic abortion cases are admitted to the gynecologic and not to the obstetric service. Two and two-tenths per cent of the hospital admissions were to the tuberculosis service and only 1.2 per cent of the cases of thrombosis were on that service.

Fatal pulmonary embolism occurred most frequently on the medical service. Of all cases of thrombo-embolism, 29.3 per cent were on the medical service, but 53.2 per cent of the fatal pulmonary emboli were on that service. The surgical service had 37.2 per cent of the cases of thrombo-embolism and 25.6 per cent of the fatal pulmonary emboli. Nine and eight-tenths per cent of the cases of thrombo-embolism were on the obstetric service, but this service had only 2 per cent of the fatal pulmonary emboli. The low percentage of fatal pulmonary emboli in obstetric patients is undoubtedly due to the fact that most of the venous thromboses on the obstetric service were thrombophlebitis, in which the clot is firmly attached to the vein wall and is not likely to become detached with the development of pulmonary infarction and death. The high incidence of fatal pulmonary embolism on the medical service is undoubtedly due to the frequency of heart disease in which mural cardiac thrombus is likely. The detachment of the mural thrombus can produce fatal pulmonary embolism.

The incidence of fatal embolism closely approximated the fatality incidence on most services with the exception of the tuberculosis and gynecologic services. The medical service had 58.2 per cent of the hospital deaths and 52.7 per cent of fatal pulmonary emboli. These respective percentages on the surgical service were 23.3 and 25.6; on the tuberculosis service, they were 11.5 and 0.5; on the gynecologic service, 1.9 and 13.8. The high fatality incidence from pulmonary embolism in gynecologic cases undoubtedly is due to the large number of suppurative thrombophlebitides in patients with septic abortion. This incidence undoubtedly will decrease from now on with the early recognition of this condition and the prompt ligation of the vena cava and ovarian veins as is practised at the present time at Charity Hospital. It is difficult to explain the relative immunity of tuberculosis patients to pulmonary embolism. It is possible that they have a relatively high blood antithrombin content.

An extremely important observation made in our previous study is that in approximately half the fatal cases there was no clinical evidence of thrombo-embolism. This is particularly significant, because almost without exception

the patients were examined for possible presence of thrombosis. Similar findings are reported by Roe and Goldthwait[6] who found in the Massachusetts General Hospital series of 92 deaths from pulmonary embolism that 53 per cent showed no clinical evidence of thrombosis or pulmonary infarction. Some fatalities could undoubtedly have been prevented had the lesion been suspected and adequate therapy, such as venous ligation, been instituted. However, because approximately half the patients with thrombo-embolism exhibit no clinical evidence of the condition even though they are carefully examined for such evidence, one cannot detect by methods employed up to the present all cases of venous thrombosis. Even prophylactic femoral vein ligation as practised so widely at the Massachusetts General Hospital did not prevent the increased incidence of pulmonary embolism as demonstrated by the findings of Roe and Goldthwait.[6]

For the past two years we have investigated the mechanism of blood coagulation with the hope that by means of a relatively simple and yet accurate method one could detect which patients are likely to develop thrombosis in order that adequate measures might be undertaken to prevent the development of venous clot. The fact that in an institution such as the Charity Hospital where for some time the staff has been interested in preventing and controlling thrombo-embolism, its incidence and also the number of deaths from pulmonary embolism has increased materially, makes it obligatory that additional measures to prevent and control the complication be developed. Since most of the fatalities are in patients with phlebothrombosis, it is these patients who require the greatest help. As mentioned previously, attempts have been made to control circulatory stasis, which is thought to be the predisposing factor in the development of phlebothrombosis of the veins of the lower extremity. Although these measures have been used for the past ten years, the desired decrease in incidence of venous thrombosis and fatal pulmonary embolism has not been obtained. It is obvious, therefore, that the predisposing factor in phlebothrombosis, *i.e.*, the increased coagulability of the blood, must be controlled.

Considerable emphasis has been placed upon the value of prothrombin determinations in indicating the presence of a thrombosing tendency. Sandrock and Mahoney[14] believe that routine prothrombin determinations postoperatively are valuable in indicating potential thrombosis. On the other hand, McClure, *et al.*[15] found that prothrombin determinations were of relatively little value. Cummine and Lyons[16] believe that the consistent finding of fibrinogen B and a short clotting time in patients with postoperative thrombosis warrant the use of these tests routinely in postoperative cases to indicate impending thrombosis. McClure, *et al.*[15] have partially confirmed the findings of Cummine and Lyons and believe that fibrinogen B determinations might be of value clinically in predicting probable thrombosis. However, we[17] have not been able to confirm the observations of Cummine and Lyons.[16]

In the investigation which we have been conducting for the past two years, there is evidence that thrombin is necessary for the conversion of fibrinogen

to fibrin possessing good tensile strength. This would suggest that phlebothrombosis does not occur unless thrombin is present to a greater or lesser degree intravascularly. Since thrombosis does not occur in every patient who has been subjected to trauma, it appears likely that normally thrombin which may be released as a result of injury following an operation or in any other way is inactivated by circulating antithrombin which combines with it. The study suggests that the circulating antithrombin may be alpha tocopherol which is normally present in the alpha globulin and gamma globulin fractions of the blood.

Antithrombin levels were obtained in patients before and on successive days postoperatively, together with prothrombin times and fibrinogen B levels; 301 surgical patients were examined in this way. It was found that if antithrombin levels were 1 to 32 or higher and continued at these levels, intravascular clotting did not occur.

The 301 surgical cases can be broken down into three groups: a control group in which no therapy was used, a group in which alpha tocopherol alone was used, and a third group in which alpha tocopherol and calcium were used. In the first or control group, there were 228 cases, of which 32 had antithrombin levels below 1 to 16 and a prothrombin value of shorter than 20 seconds (15 seconds being regarded as normal). Of this group, 19 developed thrombosis, four of which ended in fatal pulmonary embolism. There was an additional case which had a non-fatal pulmonary embolus with an antithrombin value above 1 to 16.

There were 39 cases in which alpha tocopherol alone was administered to the patients prophylactically, of which 17 had an antithrombin value below 1 to 16. Four developed thromboses, one with a fatal pulmonary embolism. One patient with a level of 1 to 16 developed a non-fatal pulmonary embolism. During the same time that the 39 cases were receiving alpha tocopherol, there were 36 cases in the above control group, 16 of which had antithrombin levels of less than 1 to 16, of which three developed thrombi and one developed a fatal pulmonary embolism. It is thus seen that the administration of alpha tocopherol alone gave approximately the same results as were obtained in the control series.

We have demonstrated by *in vitro* experiments that alpha tocopherol, when added to plasma, becomes bound by fibrinogen and other protein and does not act as an antithrombin. If, however, a trace of calcium is added to the plasma, a definite active antithrombin is demonstrated. Because of this, we have recently been using a combination of alpha tocopherol and calcium. The alpha tocopherol acetate is given by mouth when the patient is able to take it and, if the patient is unable to tolerate substances by mouth, alpha tocopherol phosphate is given intramuscularly. Ten cc. of 10 per cent calcium gluconate is given every 48 hours intravenously. There were 34 cases in which a combination of alpha tocopherol and calcium were used prophylactically. None had antithrombin levels of less than 1 to 16. There were no cases of clinically demonstrable thromboses, but there was one fatality from

pulmonary embolism. This case deserves special comment and is, we believe, an unnecessary fatality, because we placed too much dependence upon the normal antithrombin content of the blood. She undoubtedly had an undetected phlebothrombosis before alpha tocopherol and calcium therapy was instituted.

Case Report.—This patient was a 71-year-old white female with an extensive carcinoma of the lung, with considerable infection. A pneumonectomy was performed with difficulty. The postoperative course was uneventful until the second postoperative day, when oxygen administration was discontinued. Shortly after this she complained of sudden onset of dyspnea, cyanosis and showed evidence of shock. She recovered from this episode in a few moments only to have a repetition of the signs and symptoms within a few hours. It was felt that the withdrawal of the oxygen was responsible for symptoms. She was carefully examined for evidence of phlebothrombosis in the extremities and because no such evidence was found and because the antithrombin level was high, it was erroneously considered that the respiratory attack was of little significance and femoral ligation was not done. The patient did well subsequently until the seventh postoperative day when she suddenly experienced dyspnea, cyanosis, and went into shock. Cardiac function ceased, but respiration continued for a short while. All resuscitative measures failed, and she died. Autopsy showed massive pulmonary embolism of the one remaining lung. Some of the clots which were in the periphery were much older than those more proximally located and showed considerable organization, with fibrous adhesions to the vessel wall.

It is our conviction now that the patient had extensive phlebothrombosis before she was operated upon and that by the administration of alpha tocopherol and calcium a high antithrombin level was maintained in the postoperative period which gave a false sense of security as regards the presence of a clot. It is probable that following her first respiratory distress on the second postoperative day she should have had bilateral femoral vein ligation and had this been done undoubtedly the death could have been prevented. The maintenance of the high antithrombin level in the immediate postoperative period prevented the development of new thrombi.

This case illustrates the necessity of maintenance of constant vigilance, in spite of adequate levels of antithrombin in the blood, on all patients in whom phlebothrombosis might previously have developed. It is the experience of most clinicians that individuals with phlebothrombosis who are under anticoagulant therapy can have repeated pulmonary infarction and even fatal pulmonary embolism even though further coagulation of the blood is prevented by the anticoagulant. One distinct advantage of maintaining a high antithrombin level in the blood by means of alpha tocopherol and calcium administration over the use of anticoagulants is that although it appears at the present time that a high antithrombin titre will prevent a clotting tendency, it does not produce a hemorrhagic tendency as is likely when anticoagulants are administered. We have not hesitated to administer alpha tocopherol and calcium to patients who have undergone transurethral prostatic resection and to individuals with ulcerating lesions or even to those with hemorrhagic ten-

dency, including hemophilia. We have never observed hemorrhage in any of such cases.

These investigations suggest that intravascular clotting is determined by the relative disproportion between the prothrombin and the antithrombin levels of the blood and that whenever the disproportion becomes great enough intravascular clotting can occur. This undoubtedly explains why some patients with low prothrombin levels as a result of anticoagulant therapy develop thromboses, as this would be entirely possible if the antithrombin level is proportionately lower.

SUMMARY AND CONCLUSIONS

In spite of intensive prophylactic and therapeutic measures to prevent thrombosis and embolism, the incidence of venous thrombosis, non-fatal and fatal pulmonary embolism, has increased progressively in the past few years. The present investigation suggests that phlebothrombosis is the result of a relative disproportion between the prothrombin and the anti-thrombin levels of the blood and that by the correction of antithrombin deficiency which occurs in a high percentage of patients submitted to major surgical procedures the incidence of thrombo-embolism may be decreased. Antithrombin has the distinct advantage over anticoagulants in that, although it corrects the thrombosing tendency, it does not produce a hemorrhagic tendency. It must be emphasized, however, that in patients with lesions predisposing to venous thrombosis which have been existent before antithrombin administration and in whom venous thrombosis has already occurred, administration of antithrombin will not prevent the detachment of the clot. Therefore, a continued vigilance in all patients who are likely candidates for venous thrombosis must be maintained in order to detect early evidence of thrombo-embolism so that curative procedures, such as venous ligation, may be undertaken to prevent a fatality.

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DISCUSSION.—DR. ARTHUR W. ALLEN, Boston: As many of you know, for more than a decade we have been vitally interested in trying to prevent deaths from pulmonary embolism at Massachusetts General Hospital. We have had to come to conclusions similar to those of Doctor Ochsner; that in spite of a concentrated effort by a group particularly interested in this field our results have been quite disappointing.

Actually, we have had specific experience with approximately 3500 patients on whom we have tried by one means or another to prevent a fatal embolism. In more than 1500 cases the patients had already developed a thrombosis of the leg veins prior to institution of therapy, and many of them had had emboli. Those patients were all subjected to interruption of the femoral veins with removal of the clots, and in this group there were seven who died of further emboli.

We thought perhaps that in a vulnerable group of patients, particularly those with fractures of the extremities, the older patients with intra-abdominal carcinoma, etc., we could do a better job if we did a prophylactic interruption of the femoral veins. We subjected approximately 1000 of these older patients of the vulnerable type to femoral vein interruption, and five of those died of a massive embolism.

We have treated approximately 1000 patients of a suitable age group—the middle-age group—with Dicumarol in small doses, prophylactically. None of those patients have succumbed to embolism, but two have died of hemorrhage as the result of the Dicumarol. So we end up in this study of 3500 patients, all treated to the best of our ability, with a mortality rate of less than .5 per cent, which is, I think, as good as any series that has been published from any country by any individual or individuals interested in this field, with the possible exception of Murray's series treated by heparin. The expected deaths in a similar series of untreated patients would have been ten times as great.

We are perfectly certain that many lives have been saved. On the other hand, we have had many skeptics on our staff and the results of an analysis recently published in the New England Journal of Medicine by Doctors Roe and Goldthwaite, residents of our institution, are interesting. They have analyzed the autopsy material for the last decade—during the same time we have been trying to prevent people from dying of pulmonary embolism—and find, very much to our disturbance, that the ratio of people dying from pulmonary embolism to the number of patients autopsied in the Massachusetts

General Hospital has remained unchanged. In other words, 91 patients have died in the last decade in our institution from pulmonary embolism. It is only fair to state that only ten of those were treated by femoral vein interruption. The others had no specific measures taken to prevent the situation. Many of them occurred on the medical service, although the medical people have been particularly alert in their efforts to protect these patients.

We are perfectly certain that there is plenty of opportunity for further research in this field. I am not sure what is causing the increase in thromboses. I have tried to believe it was due to the increased age of the patients, to increased magnitude of the surgery and, perhaps, to the fact that people now on the surgical services rarely die of anything else.

We must develop reliable laboratory tests. Then we must have reliable methods for preventing thrombosis. It must be routine; it can no longer be selective. Whether alpha tocopherol and calcium will be the answer I do not know—I certainly hope so. We are now using this method of prophylactic treatment. Our series is too small at this time to be of statistical significance. More than 50 patients of a vulnerable type have had this drug in our hospital so far with no instance of thrombosis.

DR. WALTER D. WISE, Baltimore: I had not intended to discuss this paper and do not have our figures up to date, but I simply want to stress what I have said before here, and in a relatively recent publication, the importance of prophylaxis. That is really the way, I feel, to approach this problem. As to what the test is to be, whether an estimation of prothrombin time, or antithrombin estimations, remains to be worked out. Certainly the prothrombin estimation is difficult to interpret, there is no unanimity as to what the standards should be, although there are important committees working on that phase of the problem, and I hope something may come of their work. It is, however, a great pleasure to those of us who have been working feebly in this field to hear anticoagulant therapy spoken of so favorably—even by Doctor Allen—and I would like to call attention again to the published figures we have, and they have grown greatly since publication.

We had, when the article was published a few months ago in Surgery, Gynecology and Obstetrics (April, 1949), 3300 cases of major surgery treated prophylactically, with one death of uncertain cause. In that case the patient should not have been on the prophylactic program, for reasons given in the published paper. We get prothrombin estimations on the second or third day after operation. Our chief of laboratory, Charles Brambel, has done a good deal of work in this field, and has his own method of prothrombin time estimation, which is a modification of Quick's, and on his advice, after consultation with the surgeon in charge of the case, the dosage of Dicumarol is estimated. We do not run the Dicumarol to as heavy dosage as is the case in many clinics, for fear of hemorrhage. We believe moderate prothrombin levels are quite sufficient. Of course, in certain cases it cannot be used. We do not use it in gastric resections, and many other instances in which we would like to use it. Our program has been enlarged to include appropriate non-operative cases, and a striking thing has occurred in a small number of patients who have been overlooked. The program is carried on mostly from the operating room records—the posted cases. We have unfortunately overlooked a number of patients with fractures, crushing wounds of the chest, a few obstetrical cases and others. In these there has been a heavy incidence of thrombosis and embolism. The figures are not of sufficient size to be of value, but this number of thrombo-embolic episodes in the omitted patients has made an impression upon us.

I would like to emphasize again the value of prophylaxis with *conservative* anticoagulation. If one waits until thrombosis occurs, then the chances of preventing embolism by anticoagulant therapy are good, but, of course, prevention is better. I believe the time is approaching when we will be able to do more in the way of prevention. Whether Doctor Ochsner has the answer or not remains to be seen by further investigation, but

I think the intensive study that is going on now in that line is very encouraging and very hopeful.

We do not feel that Dicumarol is the last word. We are hoping for a more efficient and less dangerous drug.

DR. HUGH A. GAMBLE, Greenville, Miss.: I was struck by the last speaker's remarks in regard to prophylaxis. There is an old saying that an ounce of prevention is worth a pound of cure. In the early 1930s in our clinic it appeared to us that we were having an unusually large number of cases of phlebitis; in fact, in one community from which we draw a good deal of our work, the public was inclined to be hypercritical and we came in for considerable criticism. We gave this condition a great deal of serious consideration at that time and came to the conclusion, as expressed by Aschoff, that there were at least three main factors in its causation. The first and most important is that, in most postoperative cases particularly, there is retardation of the flow of blood; second, there is always a considerable loss of body fluids in any major operation with its attendant concentration and increased viscosity of the blood; and, third, that there is a decided increase in the blood platelets and those elements favoring increased coagulability.

At that time we instituted a regimen in all major operative cases in which the patient was given intravenous glucose continuously throughout the operation, usually ranging from 1000 to 2000 cc., which was usually the limit, in order to maintain the water level of the blood. Postoperatively, all patients were required to have carbon dioxide and oxygen inhalations for the first 24 hours, not to prevent pneumonia, because we did not think it had any effect upon its prevention, but to maintain a more active venous circulation by compelling the patient to take deep respirations. This was kept up for the first 24 hours, after which the patients were required to take voluntary breathing exercises. The third requirement was further stimulation of venous circulation by the use of what we have termed the "bedcycle." Many of you are familiar with it. It is two bicycle pedals mounted on a frame and placed at the foot of the bed. Beginning on the day of operation these patients are required to use the "bedcycle" twice daily. I wish to emphasize the use of this "bedcycle" on the day of operation, because those factors and elements which are responsible for phlebitis, coagulation of the blood, and formation of thrombi, are most active at that time and, in our opinion, all cases begin within the first 24 hours. This regimen is kept up for ten minutes twice a day and, in addition, the patient is ambulatory usually within 24 hours after operation.

Since 1935 we have had something over 46,000 major surgical cases. With those in which this regimen has been used we have had eight cases of phlebitis. There have been four cases of death from pulmonary embolism. One was a case of resection of the ascending colon because of cancer. The patient had expected to go home for a week but was kept at the hospital because of having had a son die of this condition. There were no symptoms until the evening before his death, which occurred on the twenty-first day following the operation. I was called about 2:00 A.M. because of the sudden collapse and dyspnea, followed by death. Autopsy showed that he had died of a pulmonary embolism which had originated in the mesenteric vessels. The second case that died postoperatively was a man who, four weeks before, had had his chin and lower lip removed because of cancer, which required considerable plastic work. The result had been excellent. He was sent back to surgery for a block dissection of one side of the neck. He was apparently in good physical condition, but about the middle of the operation his circulation went bad and the operation was rapidly concluded. Twenty-four hours later he died, and his death was shown to be due to pulmonary embolism which had apparently originated in some veins of the neck. A third case was a shotgun wound of the middle of the thigh involving both the femoral artery and vein. The patient died on the table. Autopsy showed that he had a large embolism in the right pulmonary

artery. The fourth case was a patient who had a fractured hip and, in the third week, died with all symptoms of pulmonary embolism, but we were not able to obtain an autopsy.

The point I wish to emphasize is that, since adoption of this regimen, we have had two deaths from pulmonary embolism where prophylactic measures were used, and only eight cases of phlebitis in more than 46,000 cases. In our opinion, while we do not minimize the progress being made along other lines of cure, we do believe that the physiologic approach to this subject is the most logical, taking into consideration the retardation of the blood stream, loss of fluid elements of the blood, increased viscosity of the blood and increase of those elements in the blood which determine its coagulability. The adoption of such measures as we have recommended to overcome these various physiologic causes will reduce to a minimum complications of this character.

DR. JAMES C. OWINGS, Baltimore: In the past two years, with Doctor Norwood at the Church Home Hospital, I have had occasion to treat a good many cases of leg ulcers due to phlebitis. We found in checking those cases that they all showed increased capillary fragility. In order to reverse that trend we gave these patients rutin and mixed tocopherols, and in every instance the ulcer has healed and, while taking the treatment, has remained healed.

The reason I bring this up is that I wonder, since, after phlebitis has occurred, there is increased capillary fragility, whether increased capillary fragility might be present beforehand and used as a test as to whether the patient might be going to get phlebitis. In other words, it might be wise to run this simple test in cases admitted to the hospital and, if found to show increased capillary fragility, to give them rutin and tocopherols ahead of time as a preventive measure. It is such an easy test that anybody can do it, and should it prove to be prognostic of phlebitis it might be an easy means of telling which cases are going to develop thrombosis, so that operation could be delayed for a day or two while treatment is given. I would like to see Doctor Ochsner try this if he would be willing to do so; it certainly seems to me that his paper proves, as do Doctor Allen's remarks, that operation is not the answer to this problem, and that we must develop some simple test to tell which cases are likely to get phlebitis, and treat them ahead of time.

DR. MICHAEL E. DEBAKEY, Houston, Texas: I should like to comment upon several aspects of this study which I believe deserve emphasis. First, and of particular significance, is the fact that the incidence of thrombo-embolism has continued to increase in spite of our assiduous efforts to control it. In the report which was recently made in New Orleans by Doctor Ochsner, Doctor DeCamp and me, and which is essentially similar to this one, attention was directed to several possible explanations for this increasing incidence. First, the condition may be actually occurring more frequently; second, our measures of control may be relatively inadequate; third, the increase may be more apparent than real in that with greater awareness of the condition the diagnosis is being recorded more frequently and, finally, a combination of these factors may be in operation. I believe the third factor, that is, increased awareness and greater frequency in recording the diagnosis, is of particular importance not only in contributing to the increased incidence but also in the evaluation of therapy. In a high proportion of cases, and this is especially true in phlebothrombosis, the diagnosis is little more than an assumption based upon criteria that are often vague and indefinite. Moreover, in many of these cases, unless thrombosis is demonstrated at operation or by the occurrence of pulmonary embolism, the diagnosis can never be definitely established. It is apparent, therefore, that the diagnosis may be made with varying frequency, depending upon the manner in which the clinical criteria are interpreted which, in turn, depends upon the interest and enthusiasm of the observer. As a consequence of this variability in record-

ing the diagnosis and, obviously, in its accuracy, considerable difficulty is encountered in assessing the results of a particular form of therapy on the basis of a statistical analysis of such records.

The second point which deserves further emphasis is the fact that this study has led us to develop a more critical attitude in our consideration of the problem. When we first made this study, approximately two years ago, and presented it at the Massachusetts State Medical Society meeting in Boston, Doctor Ochsner and I felt that we should not submit the paper for publication. We wanted more time to study the results of the analysis, for we were then somewhat skeptical of them. An additional two years' experience and further analysis have completely confirmed these previous observations. Whereas these findings supported some generally accepted clinical impressions concerning this condition, they negated others. Certainly they revealed good cause for dissatisfaction with our measure of control, for in almost half the fatal cases no clinical criteria or pattern of events proved useful in predicting the occurrence of the condition.

Perhaps one of the most significant observations revealed by this study is the fact that, with few exceptions, the occurrence of thrombo-embolism paralleled the distribution of the hospital population. In other words, its frequency in a particular type or group of patients was more a reflection of the distribution of these patients in the hospital than a significant characteristic of thrombo-embolism. This would suggest that thrombo-embolism is a disease entity occurring under variable circumstances and not just a complication of other disease states. This point of view may lead to a better understanding of its pathogenesis and possibly its control.

DR. ALTON OCHSNER, New Orleans (closing): I would thoroughly agree with Doctor Allen that lives have been saved and I am sure in our own institution that, although we have lost a good many patients, a good many lives have been saved by the institution of measures which he has mentioned. The fact remains that the mortality rate and the disease incidence are prohibitively high. I would certainly subscribe also to many of the remarks made concerning the value of prophylaxis; I have increasingly become convinced that prophylaxis is the most important way of combatting this condition. What is the best way to do it? I don't believe it will be anticoagulants. About two months ago at the International Surgical Society meeting at New Orleans, Gunnar Bauer, who, as you know, is an ardent advocate of the use of anticoagulants—especially heparin—in discussing the presentation of Doctor DeBakey and myself, very proudly referred to the results they have been getting in Sweden with routine use of heparin. Their incidence of fatal pulmonary embolism in postoperative cases was .013%, of which he was very proud. Our incidence, in this report—of which we are not proud—is .014%. So it all depends upon what you are willing to accept as desirable.

We fear anticoagulants. Dr. George Lilly, last spring, before the Society for Vascular Surgery, reported 12 unreported cases of fatal hemorrhage from the use of anticoagulants in the Miami area. Doctor Newell, to whom I was speaking a few minutes ago, said they had had two fatalities from the use of Dicumarol. The routine use of anticoagulants may be the answer if we can predict which patients are going to develop this condition, and that was what we thought might be the answer when we started on this study. But it seems that in alpha tocopherol—and again I would like to emphasize that this is still experimental, one has a substance which is an antithrombin and will prevent the thrombosing tendency without increasing the bleeding tendency. We do not hesitate to give this to patients with prostatic resection. Doctor Burns, of our urologic division, gives it to his patients who have had transurethral prostatectomy and he does not hesitate to give it routinely. It apparently is a substance that will prevent the thrombosing tendency without increasing the hemorrhagic tendency and, if it will do that, it is certainly a worthwhile substance.

I do not know whether there is increased capillary fragility in these patients, as Doctor Owings has suggested. We have not investigated this, but I am inclined to believe

that there is not. I am sure, with the careful examination we have made of these patients, that had there been increased capillary fragility it would have struck us. It certainly has not struck us; we have not looked for it but I assure you that we will.

I would like to call attention to the fact that if you are going to use alpha tocopherol, use a product in which the alpha fraction is assayed; the trouble with most of the tocopherols—and this is true of the mixed tocopherols—is that the assay is done for all the tocopherols and one may not get a true picture. It is only the alpha fraction of the tocopherols which is an antithrombin and unless an assayed alpha tocopherol is used, you will not know whether you are getting the right result.

When Doctor DeBakey and I made our presentation in New Orleans we called attention to the fact that there was an increase in the incidence of thrombo-embolism in an institution where we have taken steps to prevent it. We were concerned about it. We did not know to what the increase was due, and we suggested that it might be due to the routine use of antibiotics. There is some evidence to support it; there is equally as good evidence against it. On the other hand, if it were proved that it was due to the increased use of antibiotics, we should by all means continue to use the antibiotics because, had these patients not died of pulmonary embolism, certainly a much larger percentage of them would have died of infection. One reason that we are having an increased number of cases is that the incidence is greater, but it is actually more than that; it is not only the increased incidence but there is actually an increase in the number of deaths. So there is something more than just increased incidence.

I want to thank all the discussors for their kind consideration of this study, which is still in the experimental stage.

TISSUE REACTIONS TO TANTALUM MESH AND WIRE*

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AT THE MEETING of the Southern Medical Association on November 24, 1947, one of us (A.R.K.) read a preliminary report on the use of tantalum mesh in the repair of large ventral hernias, and on the use of it in repairing experimentally made defects in the abdominal wall of animals.[1] Further reports were made at the meeting of the Southern Surgical Association in 1947[2] and of both Associations in 1948.[3, 4] More than 100 cases of large ventral hernias, and of inguinal hernias (mostly recurrent) with large defects and poor tissues, have now been operated upon by one of us (A.R.K.), using tantalum mesh either to close the defect or to bolster a weak suture line after the defect had been closed. The results have been uniformly good. A further report on these clinical cases will be made soon.

The object of the present paper is to report further experimental work on the tissue reactions to tantalum mesh and wire. Preliminary reports on two phases of these experiments—the resistance of tantalum to infection, and the results when tantalum was placed next to the bowel—were made last year. We wish now to report further experimental work along the lines just mentioned, as well as experiments showing other types of tissue reaction to tantalum, and other experiments bearing on the clinical uses of it.†

I. *Effect of Tantalum Mesh Next to Bowel.* There occasionally occur cases of ventral hernias with many adhesions, which after being dissected free, leave an opening with scarcely enough peritoneum left to make a proper closure. Indeed, cases are occasionally encountered in which it is impossible to close the peritoneum. This situation also occurs at times after the removal of tumors of the abdominal wall. Experiments were undertaken to determine what would happen if a large defect in such a case were closed with a piece of tantalum mesh without any peritoneum between it and the intra-abdominal organs.

A piece of rectus muscle, including the underlying peritoneum, was resected in a dog and the defect repaired by suturing a piece of tantalum mesh to the edges of the defect. The dog was sacrificed three months later. Autopsy showed that the defect had been effectively repaired by the tantalum mesh which was thoroughly infiltrated with fibrous tissue, as reported in the early experiments.[1]

* Read before the Southern Surgical Association, Hot Springs, Virginia, December 6, 1949.

† The tantalum mesh and wire used in these experiments were very kindly supplied by Dr. H. L. Davis, Director of Experimental Research, Johnson & Johnson, New Brunswick, New Jersey. The stainless steel mesh and wire were supplied by Mr. G. A. Disbro, Vice-President, The W. S. Tyler Company, Cleveland, Ohio.

There were a few omental adhesions to the inner surface of the mesh but no bowel adhesions.

Five dogs were then operated upon in a similar manner, except that in these dogs the greater omentum and the spleen were removed so that there would be no buffer between the tantalum mesh and the intestines. Autopsies were done on these animals at times varying from two days to 18 weeks after operation. In the two dogs autopsied within a week after operation, a loop

FIG. 1

FIG. 2

FIG. 1.—Dog in which three inches of the rectus muscle on each side was resected, including the peritoneum. The omentum and spleen were also removed. The defect was repaired with tantalum mesh. The dog was killed two and one-half months after operation. This shows the mesh to have been peritonealized. There are four loops of small bowel slightly adherent to the undersurface of the mesh.

FIG. 2.—(Same as Fig. 1) Appearance after the loops of bowel have been pushed away from the undersurface of the mesh with a piece of gauze.

of bowel was found slightly adherent to the mesh by fibrinous exudate. In those sacrificed at longer intervals of time, loops of bowel were found slightly adherent to the mesh, but in all cases the adherent bowel could be pushed away with a piece of gauze (Figs. 1 and 2) and in no case was there any evidence of obstruction or other untoward effect. In one case, a lobe of the liver was rather densely adherent to the inside of the mesh.

II. *Implantation of Mesh without Sutures.* As cases occasionally arise in which it is desirable to reinforce a weak spot in the fascia, or in a suture line,

with a small piece of tantalum mesh, experiments were conducted in order to determine whether a small piece of mesh implaced in such an area would remain, without migration. In 14 dogs and rabbits a piece of rectus sheath approximately one in. square was resected and a piece of tantalum mesh, cut to fit into the defect, was placed in the area without suture. There is a tendency for the material to adhere to the tissues against which it is placed. In all cases in which this experiment was tried there had been no migration of the mesh when the animals were sacrificed from a few days to several months after its implantation.

III. *Implantation of Tantalum Mesh without Turning Edges Under.* Experiments similar to those just mentioned were conducted to determine whether there would be any untoward effect in utilizing mesh without turning the edges under. As originally used the edges were always turned under.[1] In 14 animals (dogs and rabbits) mesh was implanted, with and without suture, but without turning the edges under. In none of these animals (autopsied at periods of time varying from a few days to several months) was there any untoward tissue reaction from the sharp edges of the mesh projecting into the tissues. On the contrary, the edges were found to be thoroughly covered with fibrous tissue just as in the cases in which mesh was implanted with the edges turned under.

In the cases in which the corners were fixed with sutures, the suture pulled out of the mesh occasionally and this only when the mesh was implanted under tension. It is obvious, therefore, that if the mesh is to be implanted under tension (and this should seldom if ever be the case), the edges should be turned under so that the sutures will be placed through two layers of the mesh instead of one. Even when mesh is implanted without tension, which is the ideal method, there will always be some cases in which tension will be applied to it when the patient coughs, vomits, or strains in any way. This is especially true in large ventral hernias in which the mesh is used to repair a defect in which the fascial edges cannot be closed.

IV. *Suturing of Tantalum Mesh in Place with Silk Instead of Tantalum Wire.* When tantalum mesh was first used it was felt that wire should be used as suture material instead of silk, or any of the other usual suture materials, because the wire of the mesh might cut through any suture material except wire. If silk were used to suture mesh in place under tension, or under circumstances in which it might be placed under tension by coughing, etc., it was felt that there would be a good possibility of the silk being cut through by the wire mesh even if heavy silk were used. It was also felt that if tantalum mesh were used in places in which there would be no undue tension on it, such as in reinforcing a suture line in inguinal hernias for instance, that it could be held in place by silk sutures.

In a large number of animal experiments, tantalum mesh was sutured in place with moderately fine silk and in all cases in which there was no tension it held perfectly and worked just as well as wire.

V. *Suturing of Tantalum Mesh in Place with Steel Wire.* When tantalum mesh was first used, it was felt that wire of the same material should be used to suture it in place because of the possible electrolytic action if wire of a different metal were used. It has long been held that bone plates are loosened due to electrolytic action if screws of a different metal are used to hold them in place. As steel wire is much cheaper than tantalum wire and is often available when tantalum wire is not, it was considered worthwhile to determine experimentally whether there would be any deleterious effect from suturing tantalum mesh in place with steel wire. Four experiments were therefore conducted in which tantalum mesh was sutured in place in dogs with stainless steel wire. These animals were sacrificed at periods of time varying from 15 days to 13 weeks. In no case was there any loosening of the sutures or any other evidence of unfavorable reaction due to the contiguity of the two different metals.

VI. *Effect of Infection on Tantalum Mesh.* It is not infrequently necessary to operate on patients for ventral hernia in which the site of operation is potentially or actually infected.[4] Such cases are those in which there has recently been an abscess or other infection in or near the hernia site, cases in which there is an adjacent colostomy opening, and cases of pendulous hernias with excoriations of the skin which cannot be made to heal. In view of this it seemed necessary to determine whether tantalum mesh could be used safely in such cases, or what would result if infection ensued.

Fourteen dogs were therefore operated upon in an entirely non-aseptic manner. The skin of the dogs was clipped close with fine clippers, but not shaved and not prepared in any other way. Non-sterile instruments, gloves, and gowns were used. It is felt that these experiments are of sufficient interest to be given in detail:

Experiment No. 1 (K-53). A piece of tantalum mesh 1½ x 2½ inches was sutured to the outside of the rectus sheath, in a dog, with interrupted sutures of tantalum wire. Other sutures and ligatures were of 00 plain catgut. The wound became slightly infected but healed nicely. Forty-two days later the dog was then again operated upon in a non-aseptic manner and the old wound opened. The mesh was found to be entirely covered with fibrous tissue and there was no evidence of infection left. However, on making a deep incision down to the mesh, it was found that the fibrous tissue could be separated from the mesh with a Halsted clamp over an area approximately 1/3 the size of the mesh. There was evidence that infection might possibly have prevented the infiltration of the mesh with fibrous tissue in this particular area. Throughout the rest of the area, however, fibrous tissue had grown firmly into the mesh just as if there had been no infection present. The dog was killed four months after the original operation (2½ months after the second) and autopsy showed that the mesh everywhere was thoroughly infiltrated with fibrous tissue, without any evidence whatsoever that there had been any infection.

Experiment No. 2 (K-55). A piece of tantalum mesh was sutured to the rectus sheath as in the previous experiment. Within a few days there was a large collection of pus subcutaneously. Within two weeks the skin opened and the abscess drained itself. Following this, the wound healed nicely without further external evidence of infection. The dog died six weeks after operation, at which time the mesh was found to have been

thoroughly infiltrated with fibrous tissue, except for a small area in the center which had not been infiltrated at all.

Experiment No. 3 (K-74). A large piece of rectus muscle was excised on each side in a dog and the defect repaired with tantalum mesh sutured to its edges with braided tantalum wire. There was a thin muco-purulent discharge from the wound for a couple of weeks, but within three weeks the wound had entirely healed. The dog was killed two and one-half months after operation, at which time the tantalum mesh was found to be beautifully healed in and thoroughly infiltrated with fibrous tissue, with no evidence of infection.

Experiment No. 4 (K-76). An operation exactly like the preceding one was performed on a dog except that two inguinal operations with the insertion of tantalum mesh were also done. A week later the abdominal wound was infected and partially open, discharging pus. The dog died 12 days after operation and autopsy showed an overwhelming infection of all wounds, from which pus poured out.

Experiment No. 5 (K-79). This experiment was exactly similar to the preceding one, except that there were no inguinal incisions. The dog developed a sinus tract which persisted for four months. It was killed six and one-half months after operation, at which time the mesh was nicely healed in and there was no evidence of infection.

Experiment No. 6 (K-81). A piece of the sheath of the rectus 1 by 1 in. was resected in a dog and a piece of tantalum mesh sutured in place filling the defect. The wound healed per primam in spite of the non-aseptic manner in which the operation was performed. The dog was killed three months after operation, at which time the tantalum mesh was soft and pliable and thoroughly infiltrated with fibrous tissue.

Experiment No. 7 (K-88). A piece of tantalum mesh 2 by 1½ inches was sutured to the rectus sheath in a dog with No. 0 braided tantalum wire. A week later the wound was badly infected and open. Within a month it had entirely healed without sinus formation. The dog was killed 9 weeks after operation. The wound had healed perfectly but the tantalum mesh had become very much wrinkled, possibly due to the fact that it had been given no work to do but had simply been sutured to the outside of the rectus sheath.[5]

Experiment No. 8 (KR-11). Upper and lower midline incisions were made in a rabbit, and in each area a piece of tantalum mesh one in. sq. was sutured to the rectus sheath, that in the upper area with No. 0 braided tantalum wire; that in the lower area with silk. Both wounds healed nicely without sinus formation in spite of the non-aseptic manner in which the operation had been performed. The animal was killed 12 weeks after operation. Healing was excellent in each area. The tantalum mesh was nicely infiltrated with fibrous tissue and there was no evidence of infection.

Experiment No. 9 (KR-12). This was also done in a rabbit and was similar to the preceding one, except that right and left rectus incisions were made and the piece of tantalum mesh on the right was sutured to the rectus sheath with No. 0 braided tantalum wire, and that on the left with fine black silk. Both wounds healed nicely without sinus formation. The rabbit was killed 11 weeks after operation. Autopsy showed that the mesh was nicely healed in on both sides without any evidence of infection.

Experiment No. 10 (K-92). Right and left rectus incisions were made in a dog and the incision carried down through the sheath of the rectus on each side. On each side a piece of tantalum mesh approximately 1½ by 1½ inches was sutured over the incision in the rectus sheath. On the right side No. 0 braided tantalum wire was used as suture material but silk was used for ligatures and for closing the subcutaneous tissue. On the left side, the operation was exactly similar except that 000 chromic catgut was used for ligatures and for closing the subcutaneous tissue. Both wounds became puffy, presumably from abscess formation, but both healed without sinus formation. The dog was killed 10 weeks after operation. On the right side, where silk had been used to suture the subcutaneous tissue, there was a small granulomatous cavity but there was none on the left. On both sides the tantalum mesh was nicely healed in but the edges

were somewhat curled up on both the lateral and mesial edges on each side. This was probably due to the fact that it had been sutured to the outer surface of the rectus sheath and had not been given any specific function.[5]

Experiment No. 11 (K-133). About two inches of the rectus muscle on each side were resected in a dog and the defect repaired by suturing a piece of tantalum mesh to the edges of the defect, using braided tantalum wire as suture material. A week after operation the wound was slightly reddened and bulging. Within two weeks after operation the wound had nicely healed and remained so. The dog was autopsied two months after operation and perfect healing around the mesh was found. The mesh was very soft and pliable. The defect had been completely and strongly cured. There was no evidence of inflammatory reaction. The interstices of the mesh had been infiltrated with fibrous tissue and there was no inflammatory reaction about the braided tantalum wire sutures.

Experiment No. 12 (K-134). This was done at the same time and in the same manner as the previous experiment (except that only muscle on the right side was resected) and with exactly the same clinical result. The animal has not yet been sacrificed.

Experiment No. 13 (K-135). This experiment was similar to the preceding two. The wound became infected and dog died of inanition 20 days after operation. At the time of death the wound was nicely healed on the surface, but on being opened it was found that there was a deep abscess completely surrounding the mesh so that there was no fibrous reaction to the tantalum mesh except around the edges where it was firmly adherent to the edges of the fascia to which it had been sutured. There was no inflammatory reaction around the braided tantalum wire sutures.

Experiment No. 14 (K-136). A piece of rectus sheath was resected in a dog and the defect closed with a piece of tantalum mesh. A week later the wound was slightly bulging but apparently not infected. Sixteen days after operation the dog died of some unknown reason and autopsy showed the fibrous tissues to be growing nicely through the mesh.

The first two experiments cited encouraged one of us (A.R.K.) to operate on the types of cases cited above.[4] Two of these cases became grossly infected, but in spite of this the infection cleared up rapidly and the wounds healed with a cure of the large ventral hernias. Both of these cases were operated upon almost two years ago and are still cured. These cases, plus the experimental work cited, lead us to believe that tantalum is resistant to infection and that good healing may be obtained after its implantation in spite of gross infection.

VII. *Effect of Infection on Braided Tantalum Wire.* In nine animals (2 rabbits and 7 dogs) defects produced in fascia, or fascia and muscle, were repaired with tantalum mesh sutured in place with braided tantalum wire in a non-aseptic manner. One dog died in 12 days of an overwhelming infection. Another dog died in 20 days with a severe infection, but the sutures were holding nicely, without infection around them, in spite of the fact that the center of the mesh itself was lying in an abscess cavity. The wounds in the two rabbits healed per primam. Of the remaining five animals (all dogs), the wounds of three of them became slightly infected but healed promptly without sinus formation. In one dog a sinus formed which persisted for three weeks and then healed. In another dog a sinus persisted for four months. This dog was autopsied six and one-half months after operation, at which time the healing in of the mesh was complete and there was no evidence of

any infection whatsoever. Indeed there was no residual evidence of infection, such as scarring. The other six animals which survived the stage of acute infection were sacrificed from nine to 12 weeks after operation. In all instances there was nice healing around the mesh, which was thoroughly infiltrated with fibrous tissue. There was no residual evidence of infection either around the mesh itself or about the braided tantalum wire sutures with which it had been sutured in place.

These experiments lead us to believe that braided tantalum wire, in spite of the interstices present in the material, is as resistant to infection as monofilament tantalum wire. In one clinical case previously reported[4] heavy black silk was used to close the peritoneum in spite of the fact that the wound was known to be contaminated due to excoriations on the skin which could not be made to heal. The wound became badly infected and a sinus tract persisted for a year due to the presence of the silk. The peritoneum had not been closed with monofilament tantalum wire because it was feared that it would cut through. Braided tantalum wire was not available at the time. In future cases of this sort braided tantalum wire (which does not readily cut through) should be used in closing the peritoneum, and then the large fascial defect may be closed with tantalum mesh with impunity, in spite of the fact that it is known that the wound is contaminated. In such cases braided tantalum wire should be used as suture material and catgut as ligatures. The use of silk in such cases invites the formation of persistent sinuses.

VIII. *Effect of Infection when Tantalum Mesh is Sutured in Place with Silk.* In seven animals tantalum mesh was sutured in place with silk in a nonaseptic manner, twice in rabbits and five times in dogs. In both rabbits the wounds healed nicely without any evidence of infection, nor was there any evidence of infection when the animals were autopsied 11 and 12 weeks, respectively, after operation. One dog died 22 days after operation and autopsy revealed a large subcutaneous pocket of pus. Another dog, sacrificed ten weeks after operation, showed no sinus tract, but a subcutaneous granuloma. A dog killed 14 weeks after operation showed a granuloma one cm. in diameter next to the mesh. One killed 15 weeks after operation showed small granulomas enclosing the silk sutures. One killed ten months after operation still had a persistent sinus tract going down to a silk ligature.

These experiments demonstrate what is generally known, namely, that infection in the presence of silk is apt to cause trouble—either persistent granulomas surrounding infected sutures or ligatures, or persistent sinus tracts. It has been shown above that tantalum mesh sutured in place with either monofilament or braided tantalum wire is resistant to infection. Silk should not be used for buried sutures or ligatures when tantalum mesh is used, either in contaminated cases or in cases in which infection might possibly be expected to ensue. Were not dogs and rabbits more resistant to infection than human beings we might have expected more trouble than was encountered in the experiments recounted in the preceding paragraph.

IX. *Comparison of Resistance of Tantalum Mesh and Steel Mesh to Infection.* Three dogs were operated upon in a non-aseptic manner with the implantation of tantalum mesh on one side and steel mesh on the other. The following are the details of these experiments:

Experiment No. 1 (K-81). Right and left rectus incisions were made. A piece of the sheath of the rectus 1 by 1 inches was resected on each side. On the right side a piece of tantalum mesh was sutured into the defect, using tantalum wire as suture material. On the left side, a piece of steel (dur-loy) mesh was implanted, using stainless steel wire as suture material. Plain catgut (000) was used as ligatures and for closing the subcutaneous tissue. A week later the site of implantation of the tantalum mesh was healthy looking and flat. There was a large tumor in the area in which the steel mesh had been implanted. Two weeks later the right side was still healthy looking and flat; the left side was bulging and infected. The wound on the left side healed six weeks after operation. The dog was killed three months after operation. The tantalum mesh on the right side was soft and pliable and thoroughly infiltrated with fibrous tissue. The steel mesh on the left side was surrounded by thickened scar tissue, which, however, had infiltrated the interstices of the mesh. As will be shown below, infiltration of the steel mesh with fibrous tissue has not been the rule in the few experiments done. It is felt that in this case the presence of infection had caused more scar tissue, and probably was responsible for the infiltration of the interstices of the mesh with fibrous tissue to a greater degree than usual.

Experiment No. 2 (K-134). An experiment exactly similar to the preceding one was performed except that in each case the mesh was sutured in place with 000 chromic catgut instead of wire. A week after operation both wounds were bulging markedly, apparently with pus. There was slightly more bulging on the right than on the left but no leakage from either wound. Two weeks after operation the right side had healed, but pus was exuding from the left side. Five weeks after operation, the right side (tantalum) was still nicely healed and flat. The left side (steel) was lumpy and had a sinus tract from which pus exuded. Two months after operation the sinus tract had healed, but the site was still lumpy and deformed.

Experiment No. 3 (K-136). An experiment exactly similar to the preceding two was performed except that in this one both pieces of mesh were simply laid in place and not sutured. A week later both sides were bulging, the left more than the right. The dog died 16 days after operation. The right side was nicely healed and flat. There was slight bulging on the left side and a draining sinus. On the right side (tantalum) firm healing had taken place without any reaction and fibrous tissues were growing nicely through the mesh. On the left side (steel) the mesh was found lying in a pool of pus with no healing whatsoever and no adherence of the fibrous tissues to it.

These few experiments would indicate that tantalum mesh is much more resistant to infection than stainless steel mesh.

X. *Effect of Tantalum Mesh on Fibrous Reaction.* In the early experimental work[1-4] the impression was obtained from the profuseness of the fibrous reaction around tantalum mesh that tantalum actually stimulated the growth of fibrous tissue. Experiments have been conducted in order to determine whether this is actually true or not. In seven animals (two rabbits and five dogs), a square of rectus sheath was resected on each side and the space filled in with tantalum mesh on the right but with nothing placed in the resected area on the left. These animals were sacrificed at periods of time varying from 15 days to 13 weeks after operation. In three of them (two rabbits and one

dog) the amount of fibrous reaction seemed to be equal on the two sides. In the other four animals (all dogs) there was marked increase in fibrosis on the right side.

It has previously been shown, in connection with experiments on preserved fascia,[6] that when a portion of the rectus sheath is resected, the space will become filled with fibrous tissue spontaneously within the next few months. The experiments reported here indicate that this fibrous reaction is more prompt and more marked if the space is filled with tantalum mesh. Whether this is due to an actual chemical stimulation on the part of the mesh, or simply to its furnishing a supporting mechanical framework for the growth of fibrous tissue, has not been determined. The latter is probably the case, as tantalum mesh has generally been considered to be inert.[7, 8] Further evidence that this is true is indicated by work on tantalum in tissue cultures, not yet reported,[9] but briefly mentioned below.

XI. *Comparison of Fibrous Reaction around Tantalum and Stainless Steel Sutures.* In six animals (four rabbits and two dogs) the rectus sheath was incised on each side and on one side sutured with a running suture of tantalum wire, and on the other side with a running suture of stainless steel wire. These animals were sacrificed at intervals of time varying from one to eight weeks. Grossly very little difference could be detected between the fibrous reaction around the two different suture materials. The knot at each end of the running suture was cut in each case and the wire suture withdrawn. Microscopic sections were then made across the bed in which the suture had lain. A study of these sections showed considerably more fibrosis around the tantalum sutures than around the steel (Figs. 3, 4 and 5). On the other hand, there was more reaction immediately adjacent to the steel sutures than there was immediately adjacent to the tantalum sutures, which would seem to indicate that there was possibly a slight irritation from the steel suture that caused a reaction immediately adjacent to it (Figs. 3, 4 and 5). It is not understood why there should be more reaction of an inflammatory nature next to the steel suture and more fibrous reaction more or less away from the tantalum suture.

XII. *Effect of Tantalum Oxide Powder on Fibrosis.* Olson[10] and others[11] have stated that there is an oxide coating always present on tantalum. If this is true, whatever effect tantalum has on tissues must be due to the tantalum oxide coating as that is the part that is in direct contiguity with the tissues. A series of experiments were therefore conducted to determine what effect, if any, tantalum oxide powder would have on fibrosis. Thirteen animals were used in these experiments—five rabbits and eight dogs. In ten of the animals a piece of rectus sheath approximately 1 by 1 inches was resected on each side. On the right side, tantalum oxide powder was rubbed into the defect and nothing was placed in the defect on the left side. In the other three animals the internal oblique muscle was sutured to Poupart's ligament on each side, and on the right side tantalum oxide powder was placed over the suture line, none on the left. One of the thirteen animals died in 12 days of an overwhelming

FIG. 3 FIG. 4

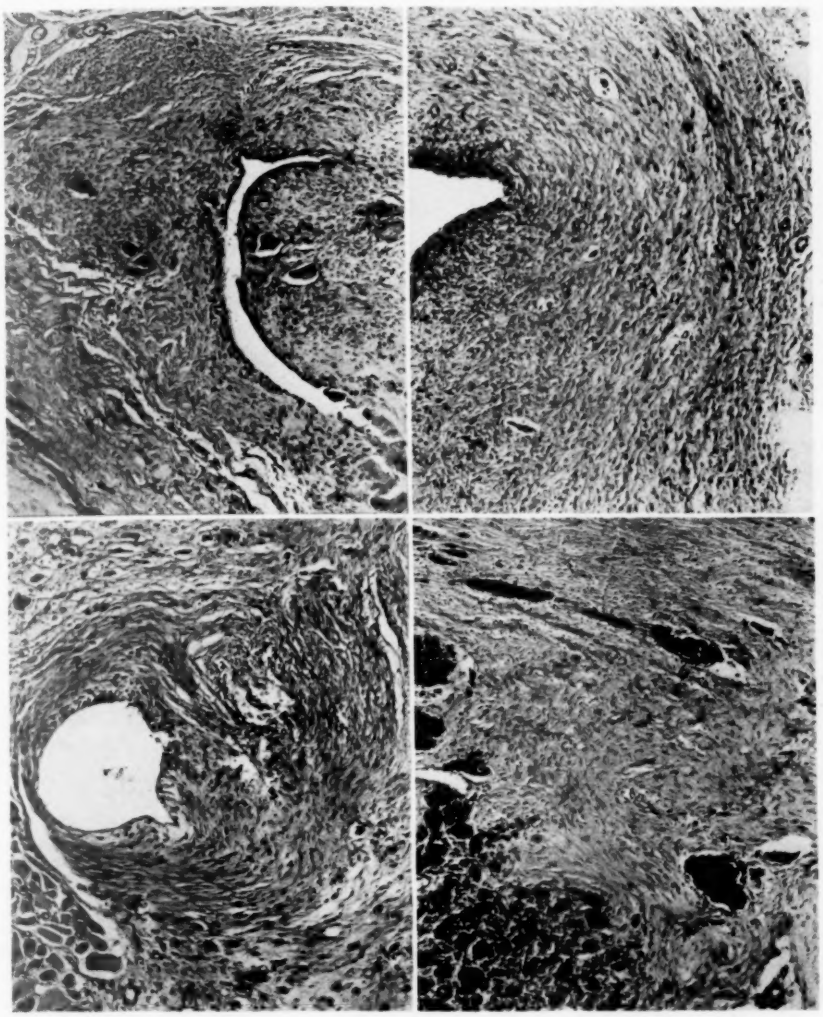

FIG. 5 FIG. 6

FIG. 3.—An incision was made in the rectus sheath in a rabbit and the incision sutured with a running stitch of tantalum wire. The animal was killed three weeks after operation, the wire withdrawn, and a section made through the bed in which it had lain. The section shows considerable fibrous reaction about the aperture.

FIG. 4.—On the opposite side of the same rabbit shown in Fig. 3, the same operation was done and the wounds sutured with stainless steel wire. This section shows a normal rectus sheath without fibrous reaction but a slight inflammatory reaction along the edge of the aperture in which the stainless steel wire had lain.

FIG. 5.—A section through the area in which the rectus sheath in a rabbit had been sutured with tantalum wire. Note increase in fibrosis around the aperture in which the wire had lain. The animal was killed four weeks after operation.

FIG. 6.—The rectus sheath was removed in a rabbit and tantalum oxide powder lightly rubbed into the muscle in the defect. The section taken five weeks after operation shows marked fibroblastic reaction about the tantalum oxide powder.

infection. (This was the only one of the 13 animals which had been operated upon in a non-aseptic manner.) The other 12 animals were sacrificed at periods of time varying from three weeks to 15 weeks. At autopsy the following results were observed:

Marked increase in fibrosis on the right	2
Moderate increase in fibrosis on the right	1
Slight increase in fibrosis on the right	7
Fibrosis equal on the two sides	1
Less fibrosis on the right than on the left	1
Total	12

Microscopically the findings were as follows:

Marked fibroblastic reaction about tantalum oxide powder (See Figs. 6 and 7)	3
Moderate increase in fibrosis	1
Slight increase in fibrosis	1
Fibrosis equal on the two sides (See Figs. 8 and 9)	4
Sections not yet studied	3
Total	12

The results of these experiments are difficult to interpret. Certainly they do not indicate any marked stimulation of fibrous reaction on the part of tantalum oxide powder. The results are inconstant and unpredictable.

XIII. *Comparative Effects of Tantalum Mesh and Stainless Steel and Dur-Loy Mesh on Fibrosis.* As tantalum is an expensive metal—much more expensive than stainless steel—it was felt desirable to compare the reaction of the tissues to meshes made of these two materials. Tantalum mesh has the advantage of greater pliability than stainless steel mesh of the same size. The cost of the material, however, is a disadvantage. It is felt that these experiments are of enough importance to report in detail.

Experiment No. 1 (K-62). In a dog a piece of both rectus muscles 3½ inches long was resected and the entire defect repaired by suturing to its edges a piece of 66 by 66 stainless steel mesh using stainless steel wire, 0.010 inches in diameter, as suture material. The dog was sacrificed and autopsied five months later. The wound had healed nicely around the mesh, but the mesh itself could be plainly seen and the fibrous tissues could be dissected away from it in what appeared to be a line of cleavage on each side. There was nothing like as much fibrous reaction about it, or fibrous infiltration through the mesh, as there is about similarly implanted tantalum mesh.

Experiment No. 2 (K-68). In a dog 1 sq. inch of the anterior sheath of the rectus was resected on each side, through a midline incision. On the right side a piece of 50 by 50 tantalum mesh was implanted in the area. On the left side a piece of 50 by 50 steel (Dur-loy) mesh was similarly implanted.* In both instances the mesh was sutured in place with fine black silk. The dog died of inanition 36 days after operation. The right side over the tantalum mesh was flat. There was a swelling on the left side over the steel mesh. On opening the wounds the piece of tantalum mesh was found to have become partially infiltrated with fibrous tissue and was nicely healed in place, but there was nothing like as much fibrous infiltration as usual, probably due to the poor condition of the dog. The steel mesh was found to be entirely bathed in a small

* In this and the succeeding experiments the tantalum mesh was made from 3 mil (0.003 in. in diameter) wire and the steel mesh from 4.5 mil (0.0045 in. in diameter) wire.

FIG. 7

FIG. 8

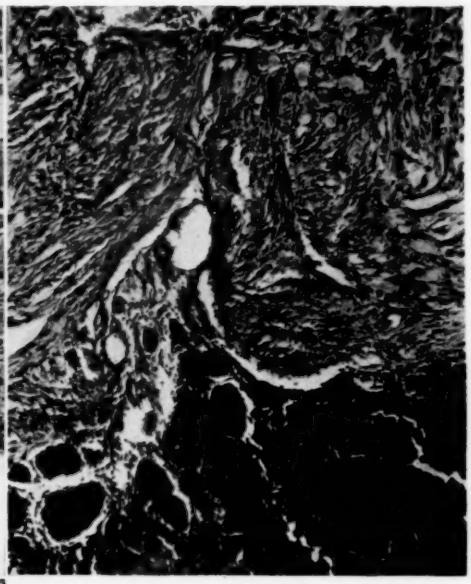

FIG. 9

FIG. 7.—Control section taken from the opposite side of the animal shown in Fig. 6. The rectus sheath was removed on this side but no tantalum powder rubbed in. The section shows normal regeneration of the sheath.

FIG. 8.—Section from rabbit operated upon in exactly the same manner as that shown in Fig. 6. There is normal regeneration of the rectus sheath but not the fibroblastic reaction shown in the other animal. The section was taken 34 days after operation.

FIG. 9.—Control side of animal shown in Fig. 8. Normal regeneration of rectus sheath is shown.

FIG. 10

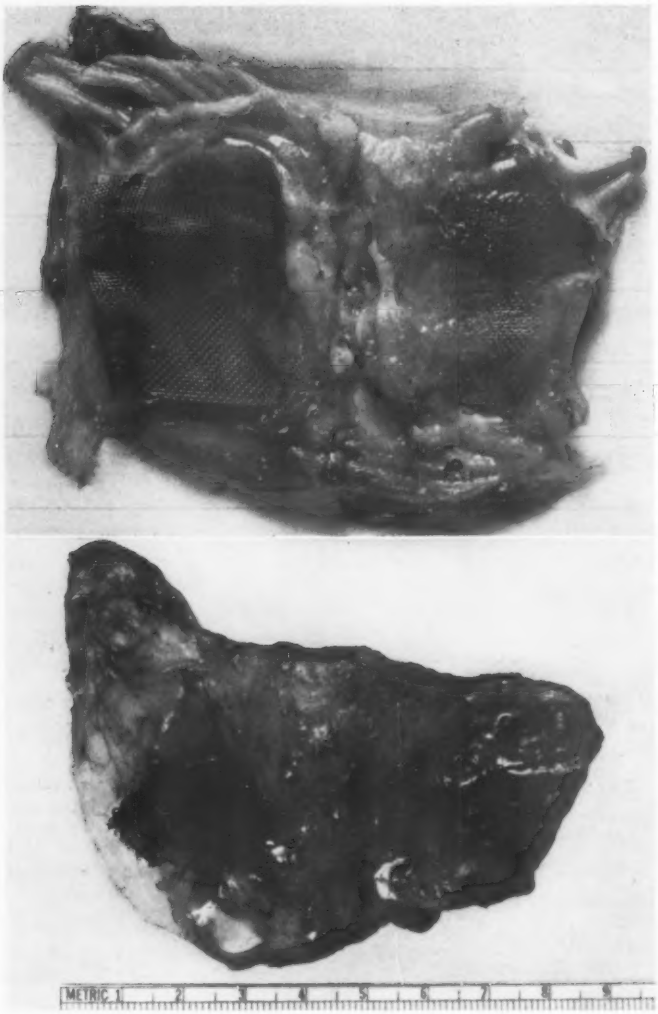

FIG. 11

FIG. 10.—A mid-line incision was made in a dog and one sq. inch of the anterior sheath of the rectus muscle was excised on each side. On the right the defect was repaired by the implantation of a piece of tantalum mesh and on the left by Dur-loy steel mesh. The dog died of inanition 36 days after operation. The site of implantation of the tantalum mesh was flat, smooth, and pliable. The site of implantation of the Dur-loy steel mesh presented a large swelling. On opening the wounds the tantalum mesh was found to be infiltrated and partially surrounded with fibrous tissue, but the fibrous reaction was not as great as usual in a corresponding length of time, possibly due to the poor condition of the dog and the fact that infection had been present. The Dur-loy steel mesh was found to be entirely bathed in a small abscess and not adherent to the surrounding tissue any place, except for a very slight attachment to the mesial edge.

(Legend for Fig. 11 on opposite page)

abscess and was not adherent to the tissues any place except for a very slight attachment of the mesial edge (see Fig. 10).

Experiment No. 3 (K-70). This experiment was exactly similar to the preceding one except that in each instance the mesh was laid in the defect without suture. The dog was killed 2½ months after operation. Autopsy showed the implanted pieces of mesh to be lying on top of each other in an abscess cavity with a draining sinus. The tantalum mesh was slightly adherent to surrounding structures. The steel mesh was simply floating in the abscess cavity. The cavity wall was greatly thickened. The migration of the two pieces of mesh was evidently due to infection.

Experiment No. 4 (K-72). A midline incision was made in a dog. A piece of the anterior sheath of the rectus 1 by 1 inches was resected on each side. On the right side a piece of 50 by 50 tantalum mesh was sutured in place with stainless steel wire. On the left a piece of 50 by 50 steel (Dur-loy) mesh was sutured in place with No. 1 braided tantalum wire. The dog was killed two months after operation. Autopsy showed the tantalum mesh to be well healed in, as usual, with no evidence of abnormal reaction whatsoever. The site of implantation of the steel mesh showed marked thickening, and on incising the area the piece of mesh was found to be encysted in a cavity containing clear fluid and the mesh was entirely free except at the lower end, where it was adherent to the tissues. The tissue around the mesh was greatly thickened and showed evidence of foreign body reaction (Fig. 11). Microscopic sections were made from tissues adjacent to both pieces of mesh. There was normal fibroblastic reaction around the tantalum mesh. Around the steel mesh there was dense scar tissue which appeared hyalinized, and there was considerable cellular infiltration.

Experiment No. 5 (KR-2). Right and left rectus incisions were made in a rabbit. A piece of the sheath of the rectus 1 by ½ inches was resected on each side. On the right side a piece of 50 by 50 tantalum mesh was sutured in place with one black silk suture in each corner. On the left side a similar piece of 50 by 50 steel (Dur-loy) mesh was implaced in a similar fashion. The rabbit was killed 62 days after operation. On the right at the site of implantation of the tantalum the wound was flat and normal looking. On the left at the site of implantation of the steel there was a large hard lump. On opening the wounds the tantalum mesh was found to be infiltrated with fibrous tissue without undue fibrous reaction. On the left side there was an enormous fibrous reaction about the steel mesh, and on cutting down to the mesh it was found to be completely surrounded by dense scar tissue without any fibrous infiltration of the mesh itself.

Experiment No. 6 (K-80). Right and left rectus incisions in a dog. A piece of rectus sheath 1 in. square was resected on each side. On the right side a piece of 50 by 50 tantalum mesh was implanted without suture. On the left side, a similar piece of 50 by 50 steel (Dur-loy) mesh was implanted in the same manner. Following operation the site of implantation of the tantalum mesh was normal-looking but a large tumor appeared at the site of implantation of the steel mesh. The dog was killed three months after operation. The site of implantation of the tantalum mesh was soft and pliable, and fibrous tissue had grown through it and around it every place. On

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FIG. 11.—A mid-line incision was made in a dog and a piece of rectus sheath one inch square resected on each side. Tantalum mesh was implanted in the defect on the right and Dur-loy steel mesh on the left. The dog was killed two months after operation and the tantalum mesh was found to have been thoroughly infiltrated and surrounded with normal fibrous tissue. On the left the Dur-loy steel mesh was surrounded by dense scar tissue, and on incising it the mesh was found to be encysted in a cavity containing clear fluid. It was entirely free except at the lower end where it was slightly adherent to the tissues.

the left side, the piece of steel mesh was encysted, and the mesh was completely surrounded by dense scar tissue which had not grown into the interstices of the mesh at all.

Experiment No. 7 (K-81). This operation was performed in a non-aseptic manner. Right and left rectus incisions were made in a dog. A piece of the sheath of the rectus muscle one inch square was resected on each side. The defect on the right side was repaired by the implantation of a piece of 50 by 50 tantalum mesh, and that on the left by the implantation of a similar piece of steel (Dur-loy) mesh. The tantalum mesh was sutured in place with tantalum wire and the steel mesh with stainless steel wire. A week after operation the right side was healthy looking and flat; the left side was bulging and infected. Two weeks later the same condition existed. Six weeks after operation the left side had also healed but was bulging, hard, and knotty. The dog was killed three months after operation and autopsy showed the tantalum mesh on the right side to be soft and pliable and thoroughly infiltrated with fibrous tissue. The steel mesh on the left side was surrounded by thickened fibrous tissue, which, however, in this instance had infiltrated the interstices of the mesh. We wonder (as indicated earlier in this paper) whether infection played any part in the infiltration in this case.

Experiment No. 8 (K-134). Operation performed in an entirely non-aseptic manner. Right and left rectus incisions were made in a dog. A piece of rectus sheath approximately one inch square was resected on each side and the defect closed on the right with a piece of 50 by 50 tantalum mesh; that on the left with a piece of 50 by 50 steel (Dur-loy) mesh. The mesh was sutured in place with 000 chromic catgut in each instance. A week after operation both wounds were bulging markedly, apparently with pus. There was slightly more bulging on the right than on the left. Two weeks after operation the right side was nicely healed and flat; the left was exuding pus. Five weeks after operation there was still a draining sinus tract on the left. Two months after operation the left side was still lumpy but the sinus tract had healed.

Experiment No. 9 (K-136). Operation in this dog was performed in a non-aseptic manner and performed in exactly the same manner as the preceding one, except that no sutures were placed in either mesh. A week after operation the wounds on both sides were bulging, the left more than the right. The dog died 16 days after operation. The right side was nicely healed and flat. The wound on the left side was bulging slightly and there was a draining sinus. On opening the wounds firm healing without any abnormal reaction was found on the right and fibrous tissues were growing through the tantalum mesh. On the left side, the steel mesh was found lying in a pool of pus with no healing whatever and with no adherence of the fibrous tissues to it.

These experiments indicate that the tissue reactions to tantalum mesh and steel mesh (Dur-loy) of approximately the same size are entirely different. Implanted tantalum mesh produces a normal fibroblastic reaction with fibroblasts surrounding and infiltrating the mesh, producing a soft and pliable wound. On the other hand, implanted steel mesh becomes surrounded with dense scar tissue which does not infiltrate the mesh and which produces a hard tumorlike effect.

XIV. *Effect of Various Metals on Tissues in Culture.* We think it is obvious from the experiments reported in the preceding four sections that there is a marked fibrous reaction around tantalum mesh and wire. It was our feeling originally from observing the results of the early experiments that tantalum actually stimulated fibrosis, possibly from the effect of some chemical

action on the tissues. It was felt that this could best be determined, however, by observing the reaction of cells in tissue culture to tantalum. As a result of this thought, one of us (A.R.K.) is now in the process of conducting experiments with Dr. George O. Gey[9] to determine the effect of various metals on tissues in culture. The results of these experiments will be reported later. Experiments done so far, however, show that cells in tissue culture grow out vigorously, not only along tantalum wire, but also along stainless steel, zirconium, and columbium wire. These early experiments would seem to indicate that none of these metals is toxic. Further experiments along the same line are being conducted and also experiments showing the effect of powdered metals on tissues in culture.

As a result of these experiments it is felt that the profuse growth of fibrous tissue through and around tantalum mesh is probably not due to chemical stimulation. But if the growth is simply due to the tantalum furnishing an inert non-irritating framework for the growth of fibrous tissue, why does not such growth also occur through and around steel mesh? There must be some delicate undetermined factor present. Possibly steel does cause some slight irritation not shown in tissue culture, such as indicated in section XI above.

XV. *Time Element Involved in the Ingrowth of Fibrous Tissue Through and Around Tantalum Mesh.* If tantalum mesh is to be used to repair defects in tissues, it is important to know how soon it may be expected that there will be a firm ingrowth of the tissues of the host through the implanted mesh. Our early experiments showed that after a few months this ingrowth of tissue was firm and solid and that the fibrous tissue incorporated in the framework of the mesh formed a very firm repair of the defect. We have now performed autopsies on 39 animals in which tantalum mesh had been implanted to repair a defect made by resecting either the rectus sheath or the full thickness rectus muscle. These autopsies range in time from eight days to six and one-half months after operation. Most of them, however, have been performed two months or more following operation. Recently we have been conducting experiments in order to determine just how soon firm fibrous reaction occurs after operation. Seven animals from these experiments have been autopsied at periods of time varying from eight days to six weeks.

The animal autopsied eight days after operation had died of an unknown cause. Two inches of the right rectus muscle had been resected and the defect repaired with tantalum mesh. At autopsy approximately one-third of the piece of implanted mesh had been infiltrated with fibrous tissue. On the left side of this animal, one sq. in. of the rectus sheath had been resected and replaced with a piece of tantalum mesh. At autopsy the mesh had been thoroughly infiltrated with fibrous tissue from the subcutaneous side but was not adherent to the underlying muscle.

Four animals were autopsied in which a defect in the rectus sheath had been repaired with tantalum mesh. These autopsies were performed 15, 16, 18, and 30 days after operation. In all of them the mesh was thoroughly infiltrated with fibrous tissue. In attempting to remove the mesh from the muscle in the

15-day animal, it was found to be so firmly adherent that it could not be removed without tearing the muscle (Fig. 12).

FIG. 12.—A piece of rectus sheath one by one and one-half inches was resected in a dog and the defect repaired by the implantation of tantalum mesh. The dog was killed 15 days after operation. A normal fibrous reaction had taken place about and through the mesh, and it had become so densely adherent to the underlying muscle that, on pulling it away, the muscle fibers were torn by the procedure.

Two animals, in which full thickness rectus muscle had been removed and the defect repaired with tantalum mesh, were autopsied three and six weeks, respectively, after operation. The one autopsied three weeks after operation was a puppy which died of inanition. Autopsy showed the mesh to be infiltrated with fibrous tissue but it was not thick. The animal autopsied six weeks after operation was one in which the operation had been done in a non-aseptic manner and in which the wound had become grossly infected but had healed without sinus formation. This animal had died of an unknown cause, and at autopsy the mesh was found to be thoroughly infiltrated with strong fibrous tissue, except at one spot in the center where there was no infiltration at all.

These experiments indicate early thorough infiltration of tantalum mesh with fibrous tissue under favorable conditions. Further experiments are being conducted in order to determine just how soon there is enough infiltration of the mesh to afford real strength to the wound.

XVI. *Effect of Implanted Tantalum Mesh on the Growth of Young Individuals.* One of us (A.R.K.) has previously reported a case of congenital absence of the abdominal wall in a four-year-old child, which was repaired by the implantation of tantalum mesh.[4] Before performing this operation, consideration was given as to what effect the implantation of the mesh would have on the growth of the child. Would there be a contracture? Similar defects were created in puppies in order to determine the results as they grew up.

However, puppies do not withstand experimental studies and laboratory life well, and the animals all died within a few weeks. It was therefore decided to operate on the child anyway. This was done more than a year and a half ago, and so far there has been not the slightest evidence of any contracture. The child had been an invalid due to his abdominal defect before operation, but since then he has been leading a normal life and playing as other children do.

However, similar experiments on puppies have been continued by one of us (A.R.K.) with the assistance of Dr. William S. Coxe.[12] (Final results to be published later.) Eleven puppies have been operated upon and in each case the anterior third of the rectus muscle was resected on each side and the defect repaired by suturing tantalum mesh to the edges of the defect. In the costal angle the mesh was sutured to the lower ribs with wire sutures going entirely around the ribs. Only two of these 11 puppies survived more than a few weeks. These were operated upon when they were three and four months old, respectively, and each operation was done seven months ago. The puppies are, therefore, now practically grown and there is no evidence of contracture whatsoever. Experiments along these lines will be continued.

Growing animals, including children, furnish striking examples of the adaptations which nature makes in overcoming apparently insurmountable handicaps. The lack of contracture in these instances are excellent examples of this principle.

SUMMARY

The results of the experimental work reported in this paper may be briefly summarized as follows:

1. Tantalum mesh placed next to bowel in closing experimentally produced abdominal defects causes no trouble other than a few light adhesions.

2. Tantalum mesh implanted without sutures, under ordinary conditions does not migrate from the site in which it is implanted.

3. Tantalum mesh may be implanted without turning the edges under, but if the edges are to be sutured, this should not be done if there is going to be any tension whatever, as the sutures may pull out.

4. Tantalum mesh may be sutured in place with silk instead of tantalum wire, but this should not be done if there is any tension, as it is possible that silk sutures might be cut through.

5. Tantalum mesh may be sutured in place with steel wire instead of tantalum wire without untoward effect or gross evidence of electrolytic action.

6. Tantalum mesh is resistant to infection, and good healing may be obtained after its implantation in spite of gross infection.

7. Braided tantalum wire is likewise resistant to infection in spite of the interstices occasioned by the braiding, which might be considered possible sites for harboring infection.

8. Silk should not be used in wounds in which tantalum mesh is used if the wound is possibly contaminated, or if it is felt that there is any chance

that infection might ensue. In infected wounds silk causes either persistent buried granulomas or persistent sinus tracts.

9. In a few experiments (three) tantalum mesh proved to be far more resistant to infection than steel mesh.

10. There is a marked fibrous reaction around and through tantalum mesh. The reasons for this are discussed.

11. There is more fibrous reaction around tantalum wire than around stainless steel wire, but more inflammatory reaction immediately adjacent to the stainless steel wire than to the tantalum wire. The reasons for this are discussed.

12. Tantalum oxide powder causes marked fibrosis about the granules in some instances, but none in others. The reasons for this are not understood.

13. Tissue reaction to tantalum mesh and steel mesh (Dur-loy) are entirely different. Tantalum mesh produces a normal fibroblastic reaction, and a soft pliable wound. Steel mesh becomes surrounded with dense scar tissue, which does not infiltrate the mesh, and which produces a hard tumor-like effect.

14. Early experiments indicate that tissues in culture grow equally well along tantalum, stainless steel, zirconium, and columbium wire.

15. Immediately upon the implantation of tantalum mesh, fibrous tissues start growing around and through the mesh. Under favorable conditions this process is complete in about two weeks, but by that time the growth of fibrous tissue is not profuse. It becomes more profuse as time goes on and is very dense at the end of two months.

16. Tantalum mesh implanted in puppies caused no contracture as the puppies grew.

As indicated in the main part of the paper, more experiments are in progress with regard to some of the points mentioned above.

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DISCUSSION.—DR. WILLIAM H. PRIOLEAU, Charleston, S. C.: I would like to present briefly with lantern slides two cases having a direct bearing upon Doctor Koontz' excellent presentation.

Case 1.—Roper Hospital No. 15153: A Negress, 52 years of age, was admitted with a large ventral hernia and a transverse colostomy. She had had resection of the rectosigmoid for lymphopathia venereum with an unsatisfactory sigmoid colostomy, and subsequent laparotomies for severing adhesions and the formation of a transverse colon colostomy. At operation through a transverse incision numerous adhesions were severed and the ventral hernia was repaired with inadequate tissue. A piece of tantalum wire mesh 11 cm. by 19 cm. was sutured over the aponeurosis; skin closure was delayed for three days. Eight days after operation 300 cc. of foul pus was evacuated from under the skin flaps. The skin sutures were removed and the wound was packed with gauze. From this time, healing took place by granulation. The skin became adherent over the mesh from the periphery. Granulations grew through the mesh and finally covered it from view. From the third postoperative day the adjoining colostomy discharged frequently and freely, constantly bathing the large open wound. The infection was localized, there being no spreading cellulitis or slough of tissues. The final healing was firm, as shown in the lantern slides.

Case 2.—Roper Hospital No. 85016: A white woman, 52 years of age, was admitted with an indurated ulcer overlying the upper portion of the sternum and the anterior portion of the first three ribs on the right, and a 5 cm. mass deeply situated in the neck superior to the medial portion of the right clavicle. Biopsy revealed neurogenic sarcoma. The onset had been ten years ago, and there had been seven previous attempts to remove it. At operation a block dissection of the lower half of the neck was performed, ligating the internal jugular and subclavian veins. The superior portion of the sternum was removed with the medial portion of the left clavicle and the anterior portion of the first four ribs on the left, and the medial third of the right clavicle and the anterior third of the first three ribs on the right. The pleura was not resected. A piece of tantalum mesh 13 by 16 cm. in size was sutured over the bony defect.

The wire mesh and the neck wound were covered with large flaps containing both breasts. A firm dressing was carefully adjusted to the optimal pressure. One week after operation the chest wall was sufficiently firm to permit the patient to breathe satisfactorily. The wire mesh was well tolerated by the tissues, and the wound was healing without gross infection.

DR. ALFRED BLALOCK, Baltimore: Before asking Doctor Koontz to close, I should like to remind you that the first use of tantalum in surgery was by Dr. John Burch, our Secretary, and Dr. Henry Carney, in about 1940.

DR. AMOS R. KOONTZ, Baltimore (closing): I am delighted that Doctor Blalock called attention to Doctor Burch's work. This work is mentioned in the paper but there was not time enough to discuss it during the presentation.

I would like to thank Doctor Prioleau for presenting his cases, which are certainly very interesting and illustrate how well this material does withstand infection. Other surgeons have had cases similarly infected in which there was perfect healing in spite of the presence of the mesh.

Since writing this paper, I have had occasion to resect a large melanoma of the abdominal wall which involved the umbilicus. The abdominal fascia, the umbilicus, and underlying peritoneum were resected, and following the resection it was impossible to close the peritoneum. On the basis of the experimental work here reported, I had no hesitancy in closing the peritoneal defect with tantalum mesh. A piece of tantalum mesh 4 by 8 inches in size was slipped in between the rectus muscle and its posterior sheath, the abdominal contents coming in direct contact with the mesh in the area in which peritoneum was lacking. So far the man has got along beautifully and I anticipate no unfavorable result.

In a number of cases with large defects this material has proved more useful than any other material which I have used, and I feel that cases have been cured with it which could not have been cured by any other means. I do not say that it is the last word. After all, it has been used for only three and a half years. There are other methods of closing defects, but I do not believe there is any other method that can be used as successfully as this in closing enormous defects in which it would be next to impossible to transplant enough fascia or a sufficiently large cutis graft.

SOME OBSERVATIONS ON THE USE OF THE COMBINED THORACICO-ABDOMINAL INCISION*

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In 1947 the usefulness of a combined thoracico-abdominal incision in the performance of splenectomy in cases with unusually large and adherent spleens was emphasized by one of us, and it was suggested that this incision should prove of value in operations involving structures situated high in the upper abdomen close to the leaves of the diaphragm. This suggestion has been followed in a total of 43 cases of varied nature all of which were operated upon by members of the Department of Surgery at the Cincinnati General Hospital including the Resident Staff. It seemed of interest to comment on the experiences gained, to present a follow-up study of this group of cases, and to mention certain changes in the original technic which have been designed to overcome the complications revealed in this study.

This type of incision gave in each case an exposure which was considered definitely superior to that which could be obtained by either an abdominal or a thoracic approach. For this reason it was possible to perform the technical details of the several operative procedures with greater ease, and what is more important, to give a wider margin to malignant lesions and to avoid excessive manipulation of the organ concerned. The time consumed in making such an incision and in closing it was more than compensated for by the ease and thoroughness with which the operation itself could be completed. It should be emphasized that in certain cases the abdominal portion of the incision should be made first to determine whether the condition is operable before the thoracic portion is undertaken. Table I indicates the types of cases in which the incision has been utilized.

Stomach. The wide exposure obtained by the incision was of great value in those cases of carcinoma of the stomach in which the extent of the lesion required a total gastrectomy or the removal of all but a tiny pouch of stomach. By means of this approach the entire stomach and its associated lymph glands, the lower one-half of the esophagus, the spleen, the pancreas, the duodenum and the transverse colon were in plain view and readily accessible (Fig. 1). The gastrohepatic ligament could be easily divided close to the liver, the coeliac axis was visualized, and the associated lymph glands could be completely removed, the duodenum could be mobilized and cut across well away from the pylorus and the stomach or, if indicated, the esophagus could be

* Read before the Southern Surgical Association, Hot Springs, Virginia, December 6, 1949.

TABLE I.—*Forty-three Cases in Which a Combined Thoracico-abdominal Incision Was Utilized.*

A. STOMACH		**D. SPLEEN**	
TOTAL GASTRECTOMY (CARCINOMA)	7	SPLENECTOMY	8
SUBTOTAL GASTRECTOMY (CARCINOMA)	3	ABANDONED SPLENECTOMY	1
SUBTOTAL GASTRECTOMY (ULCER)	3		9
EXPLORATION INOPERABLE	2	**E. KIDNEY - ADRENAL**	
EXCISION OF (LEIOMYOMA)	1	RIGHT NEPHRECTOMY (CARCINOMA)	2
	16	LEFT NEPHRECTOMY (PHEOCHROMOCYTOMA)	1
B. ESOPHAGUS			3
CORRECTION OF ACHALASIA	2	**F. PORTAL HYPERTENSION**	
RESECTION OF CARCINOMA	2	*SPLENORENAL SHUNT	2
RESECTION OF STRICTURE	1	PORTAL CAVAL SHUNT	2
	5	EXPLORATION - NO SHUNT	2
C. DIAPHRAGM		*(2 CASES INCLUDED IN SPLENECTOMY)	4
REPAIR OF STRANGULATED HERNIA	3		

G. PENETRATING WOUND
THORAX AND ABDOMEN 2

H. LIVER
PARTIAL RESECTION OF CHOLANGIOMA OF RIGHT LOBE 1

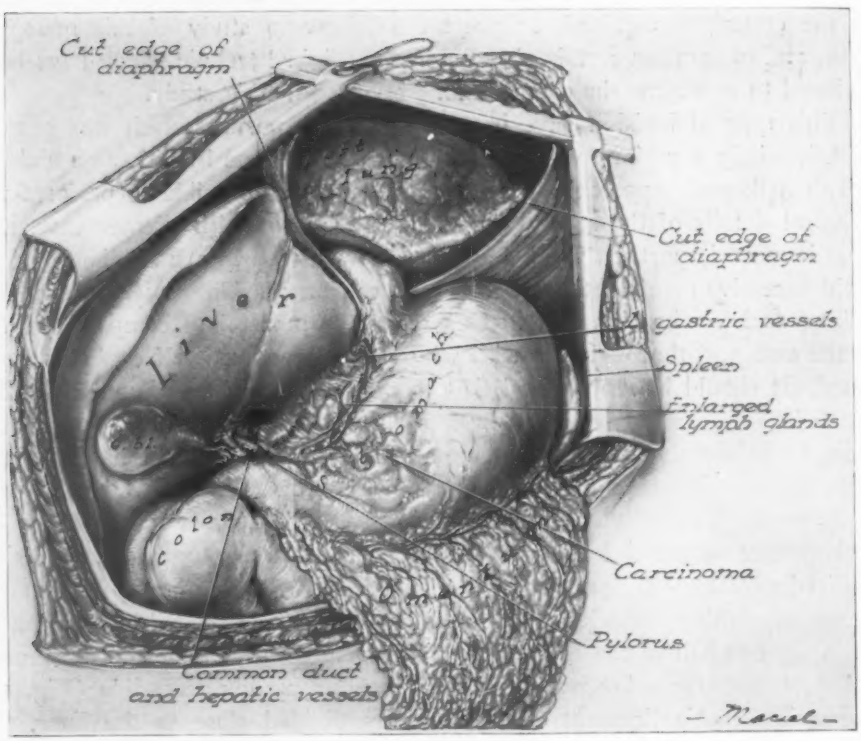

FIG. 1.—The exposure of the stomach obtained by a combined thoracico-abdominal incision.

divided at any level below the aortic arch (Fig. 2). These technical points in the performance of gastrectomy are of the greatest importance if one is to thoroughly eradicate the carcinoma in the stomach, its routes of lymphatic spread, and its extension into contiguous organs such as spleen, tail of the pancreas or transverse mesocolon. The work of Coller, Kay and McIntyre,[1] of Pack[2] and recently that of Zinninger and Collins[3] has shown that in cases of carcinoma near the cardiac end of the stomach, the malignant process

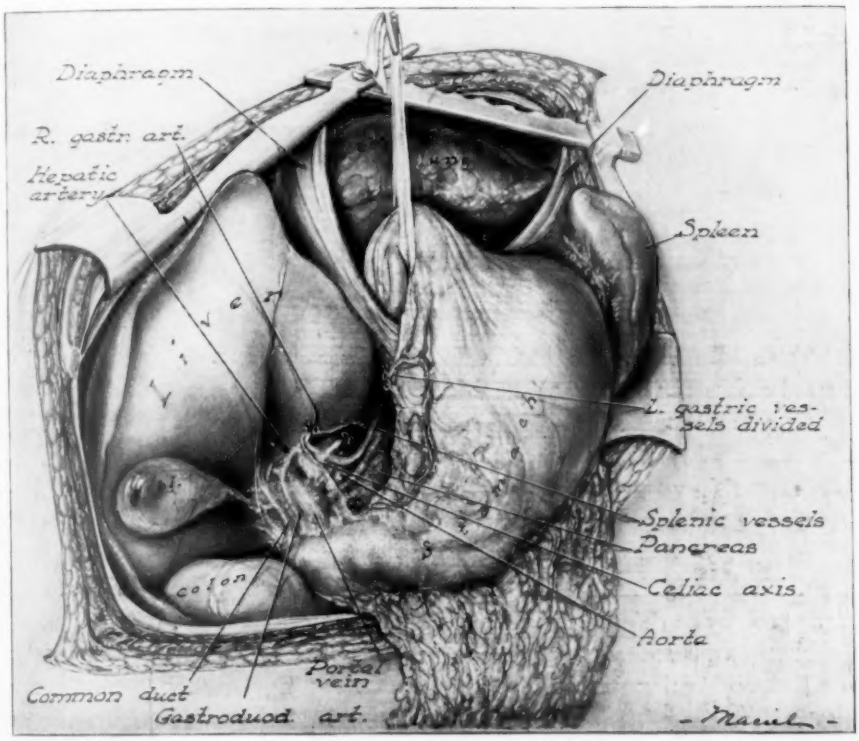

FIG. 2.—The gastro-hepatic ligament has been divided close to the liver, the left gastric artery has been ligated and the celiac axis dissected cleanly.

frequently extended well up into the esophagus even though this was not grossly evident. Consequently if the cancer is to be given a satisfactory margin it is imperative to remove a considerable length of esophagus. Whereas this is difficult or impossible through an abdominal approach it is simple through a combined one in which the thorax is widely opened. The improved exposure is of even greater assistance during the subsequent anastomosis, which is vastly easier to perform in the thorax than from below the diaphragm. For these reasons it is now our practice to employ this incision in the performance of all total gastrectomies for carcinoma of the stomach and in the majority of subtotal gastrectomies for this disease. It was utilized also in three cases of gastric ulcer which were difficult to distinguish from

carcinoma and which were situated high on the lesser curvature of the stomach. The incision proved of value in the local removal of a leiomyoma of the stomach located near the terminal esophagus and the exposure of which proved extremely difficult through the abdominal portion of the incision.

Esophagus. Two cases of achalasia, one case of stricture, and two cases of carcinoma of the esophagus were operated upon using the combined incision. Although in any of these the approach could have been transthoracic, it was felt that a combined one gave readier access and made the technical

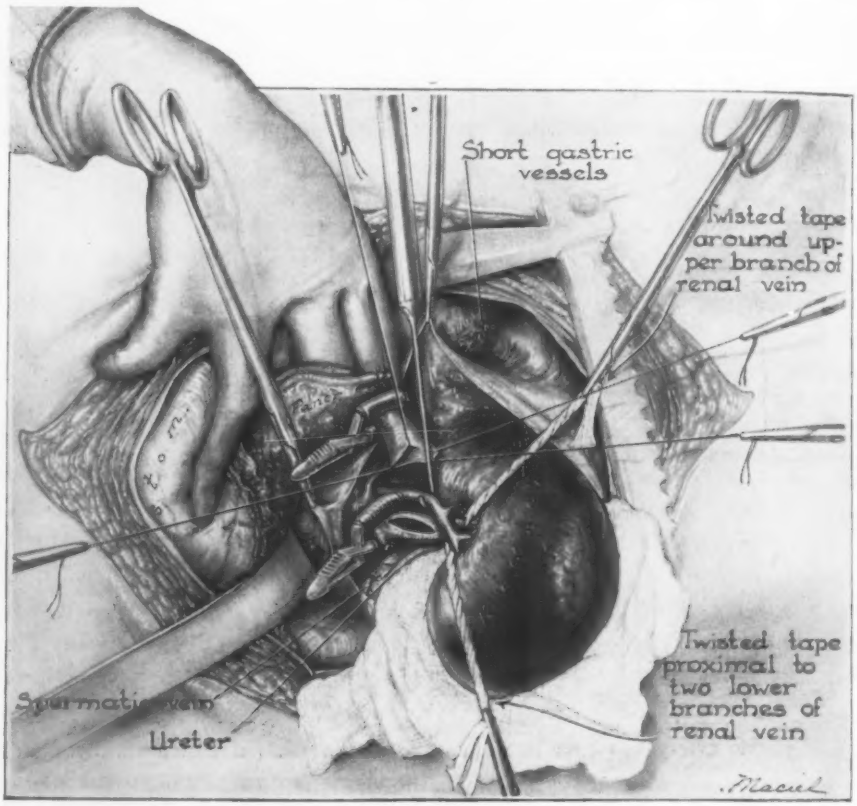

FIG. 3.—The exposure which can be obtained in the performance of a splenorenal shunt after the spleen has been removed.

procedures simpler to perform. This was particularly true in one case of achalasia where a considerable length of the terminal esophagus appeared thickened and fibrosed, necessitating the exposure of a long segment of this structure.

Diaphragm. Simple diaphragmatic hernias are in our opinion most readily approached by means of a transthoracic incision, but in those instances in which there is a strangulated and grossly distended hollow viscus the operation is greatly simplified by extending the thoracic incision across the costal

margin for varying distances into the abdominal wall, and by division of the diaphragm down through the constricting ring. This maneuver was of real value in one case in which the strangulated and gangrenous stomach filled the thorax, in another instance where a greatly distended and gangrenous loop of sigmoid occupied almost the entire left thorax and in a third case where several large loops of small intestine were incarcerated accompanied by a ruptured spleen.

Kidney and Adrenal. The incision was used in two patients with large carcinomas of the right kidney and in one instance of a huge left-sided pheochromocytoma. The chief advantages obtained were the prevention of hemorrhage by primary ligation of the renal vessels which were easily visualized, and the sharp dissection of the tumor-bearing organ under direct vision instead of by blind maneuvers and vigorous manipulation. It is believed that this approach should prove to be an important part of the technic for safe and complete removal of these types of tumors.

Spleen. Eight splenectomies were performed utilizing the combined incision. This group included two cases in which splenorenal shunts were made and one in which there was an acute rupture of the spleen. The usefulness of this method of exposure has been commented on previously and the subsequent experiences with it have served to strengthen our belief that it greatly simplifies and adds to the safety of the removal of enlarged and adherent spleens.

Portal Hypertension. The advantages of the combined incision in splenectomy obtain to even greater degree in the performance of a splenorenal shunt in cases of portal hypertension, where one must first remove a grossly enlarged and often densely adherent spleen as a preliminary procedure. It likewise permits an adequate exposure of the left kidney and facilitates its mobilization together with isolation of the renal vein (Fig. 3). For these reasons it is recommended as the incision of choice for these procedures which are at best difficult and tedious to perform. It was used with real satisfaction in two such cases which were successfully accomplished and in one case in which, owing to the anatomic arrangement of the splenic vein, the operation could not be performed.

When utilized on the right side as an approach to the vena cava and portal vein the incision provided a very satisfactory exposure and greatly facilitated the performance of a portacaval shunt in two cases. It was used in two other instances with excellent exposure but without completion of the operation due to the fibrotic condition of the portal vein. After the diaphragm has been divided, the right lobe of the liver can be dislocated upward into the thorax and the vena cava and portal vein easily brought into full view (Fig. 4).

Penetrating wounds involving thorax and abdomen. In instances in which penetrating wounds involve the thoracic and abdominal viscera the combined

incision permits access to both pleural and peritoneal cavities should such need arise due to the inadequacy of either a simple thoracic or simple abdominal approach. The thoracico-abdominal approach was found useful in two such cases in this clinic. In one of these subjected to initial laparotomy following a gunshot wound of the lower thorax with suspected injury to intra-abdominal organs it was discovered that the esophagus was perforated well above the diaphragm. The abdominal incision was extended into the thorax across the costal margin, permitting visualization and suture of the

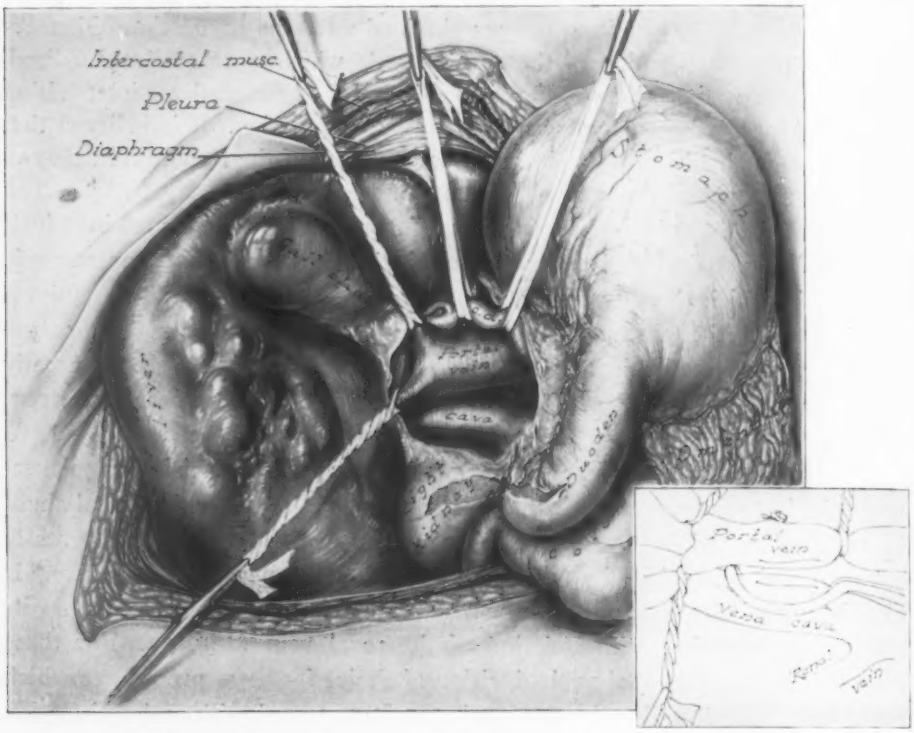

FIG. 4.—The exposure of the vena cava and portal vein preparatory to a porta caval anastomosis.

esophageal perforation. In another subjected to thoracotomy for a stab wound of the chest the diaphragm was found to be lacerated, as were the spleen and left kidney. The incision was continued across the costal margin into the abdomen, permitting the removal of the spleen and kidney.

IMMEDIATE POSTOPERATIVE COMPLICATIONS

There has not been more evidence of shock accompanying this approach than with standard incisions, and it has been remarkably well tolerated even by patients of advanced age, many of whom had neoplasms of the stomach or esophagus or were suffering from diseases of the liver and portal system. A striking feature of the postoperative period was the absence of pain refer-

able to the incision in spite of early ambulation. Postoperative pulmonary complications were no more frequent than in cases in which abdominal incisions alone were used. There were some complications referable to the pleural cavity though, except for empyema, they were not of serious moment. In two of the 43 patients a pneumothorax developed shortly after operation. One was small and was readily controlled by four aspirations but the other was a rapidly recurring tension pneumothorax which was successfully managed by the introduction of a small catheter. This complication may result from injury to the lung either during the freeing of adhesions, during the placing of the rib spreader, or from the application of undue intratracheal pressure by the anesthetist, but it is preventable by proper attention to detail. There was one instance of mediastinal emphysema. This produced no ill effect and was of interest only because of the unusual auscultatory findings. In five of the 43 cases small collections of fluid occurred in the pleural cavity. None of these was of importance and all were controlled by one or two aspirations. Empyema was a complication in two cases. In the one which ended fatally it developed early in the postoperative period and resulted from leakage in the suture line of an esophagogastrostomy. In the other case in which a portion of the colon had been resected for extension of carcinoma of the stomach, the empyema developed later in the convalescence and was attributed to failure to drain the contaminated pleural cavity. The advisability of drainage under such circumstances is now strongly emphasized. There were three instances of superficial wound infections and in one case with far advanced liver disease with ascites there was dehiscence of the abdominal portion of the wound on the tenth postoperative day.

LATE COMPLICATIONS

The late complications which might be expected to follow a combined thoracico-abdominal incision include ventral hernia, unstable costal margin, diaphragmatic hernia, constriction of the esophagus and restriction of the movements of the diaphragm. Of the 43 patients subjected to this incision 25 were suitable for follow-up studies. All of those have had a general physical examination, with especial reference to the condition of the healed incision; 17 have had complete roentgen examination of the thorax; 12 have had detailed roentgenographic studies of the esophagus, stomach, and colon and three others have had such studies of the esophagus and stomach. There was one instance of ventral hernia which was small and occurred at the site of exteriorization of a segment of devitalized colon. In two of the first few patients operated upon a separation of the costal margin developed with a resulting flare and a distinct widening of the interspace. As a result of this complication in subsequent cases considerable attention was paid to careful suturing of the severed costal margin with silk or fine steel wire after its cut edges were placed in anatomic position by means of a rib approximator (Fig. 5). Since this procedure has been adopted the costal margin has healed smoothly and firmly. In none of the 12 cases studied after barium

meal and enema was there any evidence of a hernia through the diaphragm, nor in the additional three patients in whom the stomach or esophagus were thus studied. There has been no reason to suspect such a hernia from the roentgen studies of the thorax in the 17 patients so examined. The incisions in the diaphragm of all patients were closed with simple interrupted or figure-of-eight sutures of silk and this method has proved satisfactory in view of the failure to discover any instance of diaphragmatic hernia following operation. No instance of faulty emptying of the esophagus was found in the 15 patients who were examined for this possibility and none of the 25 patients followed had complaints suggesting it. In three of the 17 patients who had roentgen studies of the thorax there was some restriction of motion of the diaphragm on the side of operation but in each of these there had been a significant degree of inflammatory reaction in the proximity of the diaphragm early in the postoperative period.

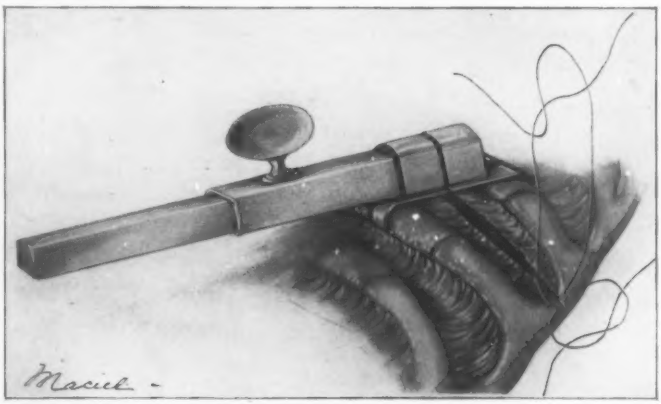

FIG. 5.—The cut edges of the costal margin have been accurately apposed and sutures of silk have been placed in them.

TECHNICAL CONSIDERATIONS

The operation originally employed consisted of a transverse incision beginning midway between the xiphoid and the umbilicus and extending across the costal margin along the eighth interspace to the posterior axillary line. It has been found advantageous to extend the abdominal incision across the right rectus muscle in patients with a narrow costal angle. If it is proposed to resect a considerable portion of the esophagus the incision is best placed in the seventh interspace as a better approach to the upper thoracic cavity is thus afforded. The intercostal incision has proved to give adequate exposure without the resection of a rib, and a Finochietto rib spreader with a long ratchet bar has made it possible to take the best advantage of the potentially wide approach. Whereas in operations on the spleen, liver, and kidney the diaphragm is best incised in the line of the skin incision, in the case of operation on the stomach or esophagus the incision in the diaphragm

should be made from the costal margin directly into the esophageal hiatus. In order to prevent the pain which occasionally is produced by irritation of the intercostal nerves, the pericostal sutures originally employed have been discontinued. Crushing the phrenic nerve to immobilize the sutured diaphragm has not been done. Incision and manipulation of the diaphragm results in a considerable restriction of its motion for a few days. Also in the interest of good pulmonary ventilation it has not been considered wise to extend the period of paralysis of the diaphragm by nerve interruption.

SUMMARY

1. Since 1947, 43 cases of varied nature have been operated upon through a combined thoracico-abdominal approach.

2. The great advantage of the incision is the wide exposure obtained which permits ease of performance of technical procedures and allows thorough removal of malignant lesions under direct vision.

3. The early and late complications directly related to the incision have been indicated. The serious ones include two cases of empyema, and two instances of instability of the lower thorax.

4. Roentgenologic study in 17 of the 25 cases which were suitable for follow-up has failed to reveal evidence of diaphragmatic hernia but has shown restriction of the movements of the diaphragm in three instances.

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DISCUSSION.—DR. ARTHUR H. BLAKEMORE, New York: We are indebted to Doctor Carter; Doctor Whipple and I were up against the problem of how best to do portacaval shunts in the early days, and had a great deal of inspiration from Doctor Carter's early work. We first started to employ the left approach, thoracico-abdominal, for splenorenal shunts; that has long since become standard procedure with us, feeling that you never do know in congestive splenomegaly just how bad the adhesions are going to be.

In about 70 cases we have done of splenorenal shunt, the majority have been by that approach. The right thoraco-abdominal approach had been a great boon to us when we decided to do more of the portal vein to vena cava type of portacaval shunt in cases of cirrhosis. The old anterior approach was a problem because of the serious disadvantage of having the risk of injury in isolating and identifying the common duct before one gets to the portal vein. The lateral, thoraco-abdominal approach eliminates this hazard. In 29 cases of portal vein-vena cava anastomoses, approximately 25 have been done by employing the right thoraco-abdominal approach. The ninth rib is resected in cases that have small livers; in those having large livers the tenth rib is removed. In cases of cirrhosis with large livers, it is usually easier to perform an end-to-side anastomosis of the portal vein to vena cava, rather than the side to side variety. In some of the cases there is a great deal of peritoneal thickening and fibrosis; particularly is this so in older cirrhotic patients who have had ascites for a long time. The lateral approach has been a great boon in this group. We feel that from the point of view of conserving blood loss and protecting the integrity of the common duct, the thoraco-abdominal

approach has contributed much to the success of portacaval shunts. We are grateful for Doctor Carter's pioneer work in the development of the thoraco-abdominal approach.

Dr. L. H. Strug, New Orleans: I am very happy to see Doctor Carter advocate this approach; although our experience is not nearly so great as his, we have found that in lesions of the upper gastric tract and the lower esophagus, the exposure this approach offers certainly warrants its use. Although many individuals have agreed with Doctor Sweet that these procedures can be performed through the transthoracic approach, the abdomino-thoracic approach offers an exposure that is a great deal more adequate. Too often many of us attempt procedures of this type through an exposure that is totally inadequate, and glory in the fact that we are able to do so; but by doing them through an exposure of the abdomino-thoracic type it is possible to carry out the procedure with greater facility.

In 12 or 13 cases in which we have employed this for upper gastric lesions, total gastrectomy, or lower esophageal lesions, we have not encountered empyema as a complication. We have had the usual pneumothorax or hemothorax, which has been controlled with repeated aspiration. I agree with Doctor Carter that it might be advisable to drain these pleural cavities through the ninth interspace, attaching the tube to negative suction, so that the lung will be rapidly re-expanded. The use of antibiotics has been a distinct aid in controlling infection in the pleural cavity. I feel that this approach definitely offers more adequate exposure, thereby facilitating the performing of these procedures so that the added time needed to open and close this type of wound does not add to the risk.

Dr. R. Arnold Griswold, Louisville, Ky.: At the Hot Springs meeting in 1944, I reported several cases in which we had resected the stomach, using a transthoracic approach without dividing the costal margin. We have since, in most such cases, come to the approach Doctor Carter has so well described. It is an approach that the abdominal surgeon may use with safety if he has adequate anesthesia administered by an anesthesiologist experienced in thoracic work; he does not have to be a thoracic surgeon. The cases in which we have used it include those Doctor Carter has described, but I think it has been most valuable to our resident staff in a large number of thoraco-abdominal gunshot and stab wounds. This is true, not only on the left, but on the right side, where the difficulties of stopping hemorrhage and bile leakage from a wound of the liver may be considerable through the conventional abdominal approach. This is a safe approach, and an approach that any experienced general surgeon can use.

Dr. Edward D. Churchill, Boston: It has been my experience that any incision through either the bed of a rib or an intercostal space must be carried back practically to where the ribs articulate with the transverse processes of the spine, if one wishes to open the door widely. I have no doubt that the thoracico-abdominal incision that Doctor Carter has shown so beautifully is excellent and adequate for the stomach and for the lower end of the esophagus. Doctor Carter made the statement that he could suture the esophagus at the level of the aortic arch. I would like to ask whether he really has a comfortable exposure for work at that level. My experience leads me to have the incision based on the transverse processes if I really want to get to the top of the pleural cavity. Doctor Carter's incision makes access to the stomach more easy than a ninth rib posterolateral incision, but for access behind the hilum of the lung or to free the esophagus from under the aortic arch, is his approach as useful as the posterolateral one?

Dr. B. N. Carter, Cincinnati (closing): I wish to thank Doctor Blakemore and Doctor Strug for their comments. In answer to Doctor Churchill, if we are doing a high esophageal resection we do prolong the incision further back toward the spine and may even, under those circumstances, have to resect a segment of the ribs above and below to get a wide exposure.

EXTERNAL ENDOMETRIOSIS — THE SCOURGE OF THE PRIVATE PATIENT*

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THE FIRST OF SAMPSON'S series of reports[1] on endometriosis in 1921 stimulated interest in this neglected disease, and in the 27 years since then there has been a progressive awakening to its diagnosis, pelvic devastating and sterilizing character, and treatment. Each of the theories of origin has its advocates, but even Sampson, the father of the appealing mechanical "retrograde menstruation" theory, for many years before his death admitted that no one explanation could be given for the origin of all cases of endometriosis. The reader is referred to the recent article by Ranney[2] for a clear and complete discussion of the various ideas, theories, and supporting facts concerning the etiology of endometriosis.

There have been numerous clinical surveys of endometriosis (Keene and Kimbrough,[3] Counseller,[4, 5] Payne,[6] Fallas and Rosenblum,[7] Holmes,[8] Hayden,[9] Sanders,[10] Fallon *et al.*[11] and Meigs.[12] From clinical experience and voluminous literature gynecologists develop impressions of the clinical aspects of this disease, many of which are of doubtful veracity. This series is compiled and analyzed in an effort to give a more definite answer to these impressions.

MATERIAL

Uterine adenomyoma and adenomyosis, commonly called internal endometriosis, are not considered in this group. It is apparently a different disease, bearing no constant relationship to external endometriosis and almost certainly of different histogenesis. As Cullen ably demonstrated in 1908,[13] it is an endometrial burrowing of the uterine wall from within. Five hundred and thirty cases of uterine adenomyoma and adenomyosis were encountered in the gynecologic pathology laboratory of The Johns Hopkins Hospital during the 15 year period from 1933 through 1947. Sixty-three or 11.9 per cent of these cases also showed external endometriosis.

Five hundred and sixteen cases operated upon in the gynecologic operating rooms of this hospital from 1933 through 1947 showed *pathologically proved* external endometriosis. Only one case is counted twice, a fact that suggests the infrequency of subsequent operations in this clinic when conservative surgery is done. During this same period 197 additional cases were diagnosed as having external endometriosis at the operating table for which there is no pathologic proof. Proof was lacking either because a biopsy specimen was not taken or because the condition was mis-diagnosed at the operating table.

* Read before the Southern Surgical Association, Hot Springs, Virginia, December 6, 1949.

A sterile safety pin inserted into the suspicious area at the time of operation makes it much easier for the pathologist to confirm the operator's diagnosis by proper sectioning. A corpus luteum hematoma was the most frequent gross lesion confused with endometriosis. In our experience these 197 cases were almost counterbalanced by 158 cases which were diagnosed in the laboratory alone. These represent 30.6 per cent of the total 516 proved cases.

TABLE I.—*Incidence in Gynecologic Abdominal Operations.*

Case Group	Number	External Endometriosis	Percent
White private gynecologic abdominal operations	1,881	299	15.9
White ward gynecologic abdominal operations	1,861	60	3.2
Colored gynecologic abdominal operations	5,047	136	2.7
Total	8,789	495	5.6

IS ENDOMETRIOSIS PRINCIPALLY A DISEASE OF THE HIGHER SOCIAL AND ECONOMIC LEVELS OF SOCIETY?

Meigs in 1941 found 28 per cent histologically proved cases of endometriosis in 400 private gynecologic abdominal operations as compared to 5.8 per cent in 400 similar public ward operations. Every gynecologist who has had ward and private practice experience confirms this discrepancy, and, despite Meigs'[12] explanation by delayed childbearing in the private patients, it remains one of the greatest enigmas of the disease.

TABLE II.—*Percentage of External Endometriosis in Pelvic Laparotomies, by the Year.*

Patient Group	1933	1934	1935	1936	1937	1938	1939	1940
Private	7.5	9.3	11.3	9.8	8.3	11.9	7.4	15.0
White ward	2.6	8.8	5.3	2.9	4.1	5.2	0.9	0.9
Colored	2.4	3.8	2.9	1.9	1.8	3.3	3.5	0.6
All	3.2	5.8	4.8	3.4	3.6	5.4	4.0	3.6

Patient Group	1941	1942	1943	1944	1945	1946	1947
Private	17.3	15.7	25.2	22.4	17.2	21.3	21.6
White ward	4.3	1.8	2.0	5.2	2.6	1.7	0.5
Colored	2.4	2.6	2.3	0.9	3.7	2.7	5.3
All	5.6	5.1	7.2	6.6	6.9	7.2	9.0

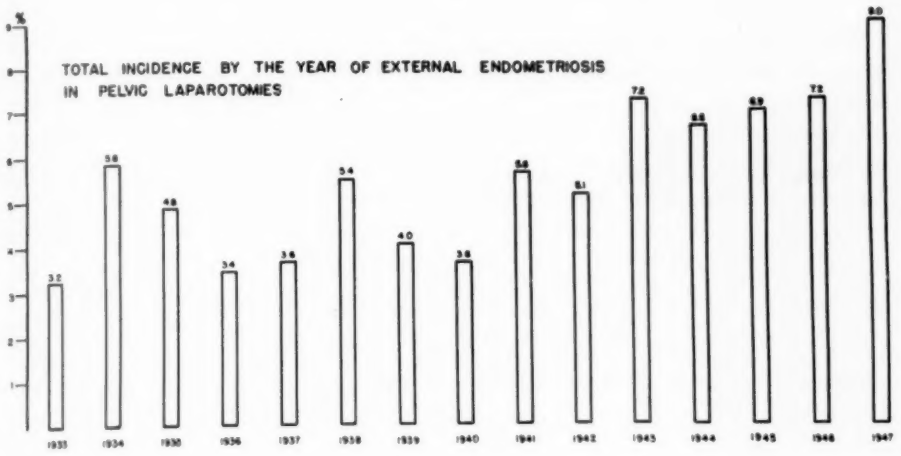
Four hundred and ninety-five of our 516 cases had gynecologic laparotomies, and in this 15-year period 8789 pelvic laparotomies were done, making a total incidence of 5.6 per cent of external endometriosis. These are divided as shown in Table I.

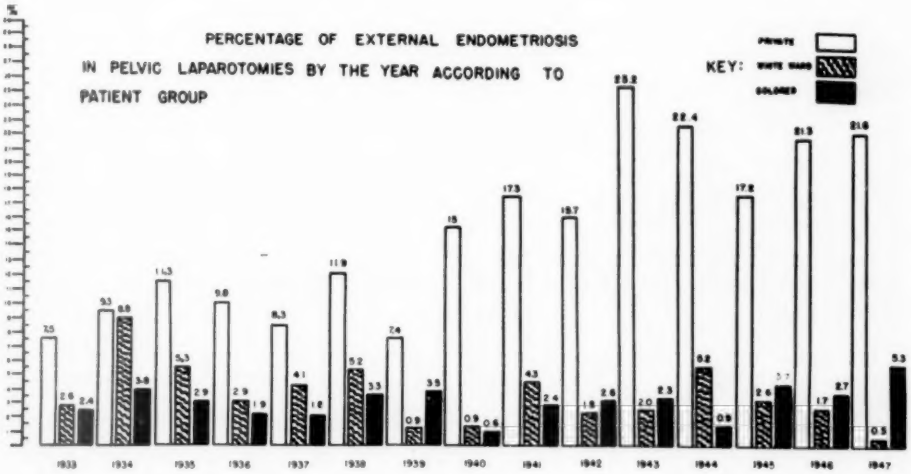
IS THE INCIDENCE INCREASING?

Gynecologists are certainly recognizing external endometriosis more frequently both preoperatively and at the operating table. That this is a true increase and not just an increase in awareness is borne out by the yearly study of the percentage of external endometriosis in pelvic laparotomies.

There has been no consistent change in the incidence among the white ward and the colored patients, but the increase from 3.2 per cent to 9.0 per cent, as shown in Table II and Chart I-A and I-B, is almost entirely accounted for by the increased frequency in private patients. Twenty-one and six tenths

A





B

CHART I.

per cent of the gynecologic laparotomies on private patients in 1947 revealed external endometriosis.

No explanation for this increase is tenable. Late childbearing with a long interval of uninterrupted menstruation, the explanation favored by Meigs and others, has not become three times as fashionable in the past 15 years.

In fact, earlier marriages and childbearing have been the rule since Pearl Harbor. Possibly more than passing consideration should be given to the dietary habits or the emotional and environmental changes incident to the larger pocketbook.

IS SYMPTOMATIC ENDOMETRIOSIS DEMANDING OPERATION FOUND IN A YOUNGER AGE GROUP THAN ALL CASES REVEALING ENDOMETRIOSIS?

The pathologic physiology of the disease demands that its symptoms be primarily confined to the menstruating period of the life cycle. Any analysis of all cases of endometriosis will include many in which the process is entirely incidental or postmenopausally inactive. For this question and subsequent questions, the total group of 516 cases was considered and a second group of 243 of these cases was separately studied. This second group includes only those cases, as interpreted from the history and operative findings, that were operated upon primarily because of endometriosis, and it will be termed the "Primarily Endometriosis Group."

TABLE III.—*Age.*

Age	Total Group—516 Cases		Primarily Endometriosis Group—243 Cases	
	Number	Percent	Number	Percent
20 or under	4	0.8	4	1.6
21–25	37	7.2	34	14.0
26–30	64	12.4	44	18.1
31–35	108	20.9	63	26.0
36–40	129	25.0	57	23.5
41–45	90	17.4	21	8.6
46–50	61	11.8	17	7.0
51–55	18	3.5	3	1.2
56–60	3	0.6	None	
Over 60	2	0.4	None	

Three patients were 19 and one was 20 years old. The oldest patient was 78, and she had an inactive area of endometriosis in an atrophic ovary, the other ovary containing an epidermoid carcinoma arising in a dermoid cyst. Thirteen of the total group were postmenopausal, ranging from six months to 25 years, but in the group operated upon primarily for endometriosis there was only one postmenopausal patient. In view of the large number of asymptomatic endometrial cysts and the increasing popularity of routine pelvic examination, it is surprising that more postmenopausal endometrial cysts are not encountered. Once a cyst is palpated in these elderly patients, the suspicion of cancer is great and removal is mandatory. Do these endometrial cysts completely collapse and disappear after the menopause, or are the walls so thinned and epithelium so flattened that histologically they must be classified as serous cysts?

Table III shows the greatest frequency of occurrence to be between 31 and 40 years of age in both groups. However, there is a higher incidence of cases operated upon primarily for endometriosis in the first half of this decade.

Thirty-eight of the 41 patients 25 years of age or younger were operated upon because of symptoms of endometriosis. This age incidence is approximately the same as found by the numerous other investigators.

WHAT IS THE RELATIVE AND ABSOLUTE STERILITY RATE OF THESE PATIENTS?

Reynolds and Macomber[14] give 12 per cent as the expected normal absolute sterility rate and Whelpon and Kaiser report it as 9.8 per cent in their Indianapolis study.

In endometriosis cases Counseller[4] reported an incidence of 32.1 per cent absolute sterility and 48.9 per cent relative sterility; Payne,[6] 40 per cent absolute; and Haydon,[9] 53 per cent relative. Numerous factors operate to make pregnancy difficult for these patients. Despite the fact that the tubes are usually patent, periovarian and peritubal adhesions, together with the resulting changes in the tubal wall, must disturb the physiology of the ovum escape and migration. The frequent association with other pelvic pathologic lesions no doubt plays a part, as does the dyspareunia of endometriosis and of the frequently complicating retro-displaced uterus. In addition, there may be other factors as yet unexplained, but related to the abnormal physiology which initiates the disease process itself.

TABLE IV.—*Sterility Rate.*

Type	Total Group Married—430 Cases	Primarily Endometriosis Group—Married—206 Cases
Relative	46.0%	41.3%
Absolute	33.5%	32.0%

Table IV shows that in our total group the relative sterility was 46.0 per cent and the absolute sterility 33.5 per cent. When most of the associated pelvic diseases are eliminated by considering the primarily endometriosis cases, the percentages are 41.3 and 32.0 respectively. These rates are probably higher than the true figures for endometriosis sterility because of possible male sterility, and in addition the histories are not entirely adequate in reference to the use of contraception. Only 27 of the 430 married patients in the total group and 20 of the 206 married patients in the primarily endometriosis group gave sterility as a major symptom. In addition, one unmarried colored girl offered this complaint as a major one. A large number of women must accept this childless state as God's will or fate's bidding until the element of pain presents itself.

IS THE TIME INTERVAL FROM THE LAST PREGNANCY TO OPERATION OF ANY VALID SIGNIFICANCE?

Fallon[11] has accented Meigs' belief by the demonstration in his group of cases that five years of menstruation without pregnancy preceding the development of the endometriosis was almost a constant factor and a valuable diagnostic aid.

In the present series, 49 of the 206 married patients with term deliveries had a pregnancy five years or less before operation. Of these 49 patients, four

were pregnant at the time of operation, three intra-uterine and one tubal. Eighteen of these 206 married patients had four or more term deliveries, and one of these had 12 term deliveries. These 12 term deliveries are certainly more than even the most ardent advocate of frequent childbearing could ask for, yet it did not prevent her from developing endometriosis.

IS UTERINE BLEEDING A PROMINENT SYMPTOM OF ENDOMETRIOSIS?

Textbooks and journal reports list abnormal uterine bleeding as the second or third most common symptom of endometriosis. Holmes[8] found some variety of abnormal bleeding in 64.9 per cent of his cases. Counseller[4] and Payne[6] report 65.6 per cent and 56 per cent, respectively, with abnormal menstruation, and both of these observers attribute this in the main to the frequently associated lesions in the pelvic organs.

TABLE V.—*Abnormal Uterine Bleeding.*

Type	Total Cases 516		Primarily Endometriosis Cases—243	
	Percent		Percent	
Menorrhagia—Total	22.4		10.2	
With other obvious cause		8.9		1.6
With other debatable cause		11.6		4.5
With no other cause		1.9		4.1
Metrorrhagia—Total	8.7		9.0	
With other obvious cause		3.3		1.2
With other debatable cause		2.5		1.6
With no other cause		2.9		6.2
Meno-metrorrhagia—Total	13.0		7.4	
With other obvious cause		7.2		1.2
With other debatable cause		3.9		2.1
With no other cause		1.9		4.1
Total	44.1		26.6	

Table V does not include the three cases of postmenopausal bleeding, three cases of oligomenorrhea, four cases of amenorrhea and seven cases of scar, umbilical and other extrauterine endometriotic bleeding. Forty-four and one-tenth per cent of the total cases and 26.6 per cent of the primarily endometriosis cases revealed abnormal bleeding. However, only 6.7 per cent and 14.4 per cent, respectively, had no obvious or debatable explanation other than endometriosis for the bleeding. By eliminating in this manner the cancers, myomas, polyps and other associated lesions, it would be fair to estimate that not more than 15 to 20 per cent of the endometriosis cases have menorrhagia and/or metrorrhagia as a symptom dependent upon this disease process alone. This may be a manifestation of ovarian dysfunction or in an occasional case of metrorrhagia may represent retrograde flow via patent tubes from intraperitoneal hemorrhage. As Fallon[11] says, change in time or amount of menstrual flow is of no diagnostic value in endometriosis, but it does help to bring to the physician the patient who recognizes irregularity as pathologic.

HOW SIGNIFICANT IS ABDOMINAL PAIN OR ITS ABSENCE?

Lower abdominal pain and dysmenorrhea have been consistently given as the most prominent symptoms of endometriosis. The lower abdominal pain characteristically begins just before or at the onset of menstruation, and may vary from a vague heavy, or bearing down, feeling in the pelvis to a sudden, severe pain indistinguishable from that experienced in other surgical abdominal emergencies. An acquired dysmenorrhea or dysmenorrhea of increasing intensity has been stressed so frequently that it is considered by many clinicians as pathognomonic of endometriosis.

TABLE VI.—*Lower Abdominal Pain.*

Total Cases 516		Primarily Endometriosis Cases—243	
Related to Menses Percent	Unrelated to Menses Percent	Related to Menses Percent	Unrelated to Menses Percent
16.3	35.5	19.8	37.9

By studying the total cases, and the individual cases operated upon primarily because of the endometriosis, it was thought that a rough elimination of most of the associated pelvic lesions could be made and a significant increase in the pain or dysmenorrhea noted. The increase of lower abdominal pain from 51.8 per cent to 57.7 per cent and the slight increase in all types of dysmenorrhea by such a comparative study were not thought to be of practical significance. The relationship of the pain to menstruation and the incidence of increasing and acquired dysmenorrhea in endometriosis are frequent and important symptoms in endometriosis, but since they are also common symptoms of other pelvic diseases, arm chair diagnosis on this basis alone is not warranted. In most of these cases there are separate histories in the record obtained by two or three different individuals, so that the incomplete or insufficient patient history was a rare finding and the study may be considered reasonably accurate. It is interesting that in the entire group 139, or 26.9 per cent, had no pain of any type and 70, or 13.6 per cent, additional, had no pain except dysmenorrhea. The not uncommon finding of extensive ovarian and/or pelvic endometriosis which is absolutely asymptomatic will continue to belie the most dogmatic exponent of characteristic signs and symptoms.

TABLE VII.—*Dysmenorrhea.*

Type	Total Cases 516		Primarily Endometriosis Cases—243	
	Number	Percent	Number	Percent
Primary—unchanged or diminishing	242	47.0	125	51.4
Primary—increasing	92	17.8	47	19.3
Acquired	39	7.5	22	9.1
None	120	23.3	40	16.5
No mention	23	4.4	9	3.7

ARE THERE ADDITIONAL SYMPTOMS OF IMPORTANCE?

As the complaints were often multiple or incidental, symptoms ranged from headaches to swollen ankles. The following symptoms and their incidence were thought to be of some importance.

Complaints of indigestion, flank pain, general fatigue and nervousness were infrequent. Three cases had rectal bleeding and two cases hematuria at menstruation and mention should be made of the painful swelling and occasional bleeding from the scar, umbilical and inguinal nodules.

Backache, sterility, pain in the rectum and dyspareunia were more frequent in those cases primarily operated upon because of endometriosis. Dyspareunia is almost certainly a more frequent symptom than noted above, for the symptom is rarely spontaneously given and the specific question is rarely asked during routine questioning.

TABLE VIII.—*Other Symptoms.*

Symptom	Total Cases 516	Primarily Endometriosis Cases—243
	Percent	Percent
Abdomen enlarging or palpable tumor	18.8	7.8
Backache	10.1	12.3
Urinary symptoms	7.6	7.4
Sterility	5.2	8.2
Leukorrhea	5.2	4.5
Pain in rectum	2.1	4.1
Dyspareunia	1.7	3.3
Found on routine examination	5.8	5.8

WHAT IS THE LOCATION OF ENDOMETRIOSIS?

The numerous reports have been in accord that the ovaries, cul-de-sac and ligaments of the uterus in that order are the most frequent sites of external endometriosis. The inclusion of adenomyoma and adenomyosis in these listings has tended to confuse them.

In Table IX the location was obtained from the operative note and the pathologic studies. Unless the operative note was specific, the small lesions were listed under the diffuse, scattered pelvic classification. For this reason the incidence for the uterine surface, posterior cul-de-sac, the uterosacral ligaments and the round ligaments may seem less than usual.

Ovarian endometriosis or endometrial cysts were found in 79.8 per cent of the total cases. They varied in size from microscopic to endometrial cysts reaching to the costal margin and containing over 2500 cc. of dark, chocolate fluid. The usual ovarian lesion was described as walnut, egg or lemon in size, but in six cases the cyst was palpable to above the level of the umbilicus. In four cases the endometrial cysts had become secondarily infected to form abscesses.

Twenty of the 37 rectovaginal nodules extended into the rectosigmoid, and there were four separate sigmoidal infiltrations. In none of these cases was

intestinal resection or colostomy necessary. Nine of the rectovaginal nodules had extension into the vagina. Five anterior cul-de-sac nodules extended into the bladder musculature.

Five of the 13 cervical endometriosis cases had previous surgery on the cervix, and only two cases had neither previous surgery nor pregnancies with vaginal deliveries. Five of these cases revealed endometriosis elsewhere in the pelvic region.

There are four cases of endometriosis in scars. One followed three years after the third cesarean section, the second five years after a cesarean section,

TABLE IX.—*Location of Endometriosis.*

Type	Site	Number	Percent*
	Ovary—one	285	55.2
	Ovary—both	127	24.6
Superficial and small spots	Diffuse scattered pelvic	171	33.1
	Uterine surface	73	14.1
	Tubal surface	71	13.7
	Posterior cul-de-sac	24	4.7
	Uterosacral ligaments	19	3.7
	Anterior cul-de-sac	11	2.1
	Omentum	3	0.6
	Round ligaments	2	0.4
	Broad ligament	1	0.2
	Small intestines	1	0.2
	Appendix	7	1.4
Abdominal nodule	Rectovaginal septum	8	1.6
	Rectovaginal with rectosigmoid involvement	20	3.9
	Rectovaginal with vaginal extension	9	1.8
	Sigmoidal	4	0.8
	Anterior cul-de-sac	2	0.4
	Anterior cul-de-sac with vesical involvement	5	1.0
	Tube	8	1.6
	Broad ligament	4	0.8
	Round ligament	3	0.6
Others	Cervix	13	2.5
	Inguinal	4	0.8
	Umbilicus	4	0.8
	Incisional—ventral	4	0.8
	Incisional—vulva	1	0.2

* The total amounts to more than 100% because of multiple lesions in many cases.

the third 12 years after a bilateral salpingectomy for pyosalpinges and the fourth 13 years after a right salpingo-oophorectomy, left salpingectomy and a fundectomy for tubo-ovarian abscesses. In none of these was continuity demonstrated between the scar endometriosis and the uterine incision. One vulvar endometriosis developed in the scar of a previous Bartholin gland excision. Of the four cases of umbilical endometriosis only one had previous gynecologic surgery, and the scar did not extend to the umbilicus. Pelvic endometriosis was found in only one of the four cases with umbilical lesions. Three of the inguinal endometriosis cases involved the inguinal portion of the round ligament and the fourth was an endometrial cyst of the Canal of Nuck.

ARE ASSOCIATED PATHOLOGIC FINDINGS OF ANY RELATIVE SIGNIFICANCE?

The 57.4 per cent incidence of myomas is approximately the same as reported by others (Counseller,[4] Payne,[6] Holmes,[8] Haydon[9]). Myomas and endometriosis are commonly associated with infertility and have been considered by some observers as resulting from increased estrogen secretion. Since endometrial hyperplasia was found in only 13 of the 516 cases, this hypothesis cannot be confirmed pathologically, and it has not been substan-

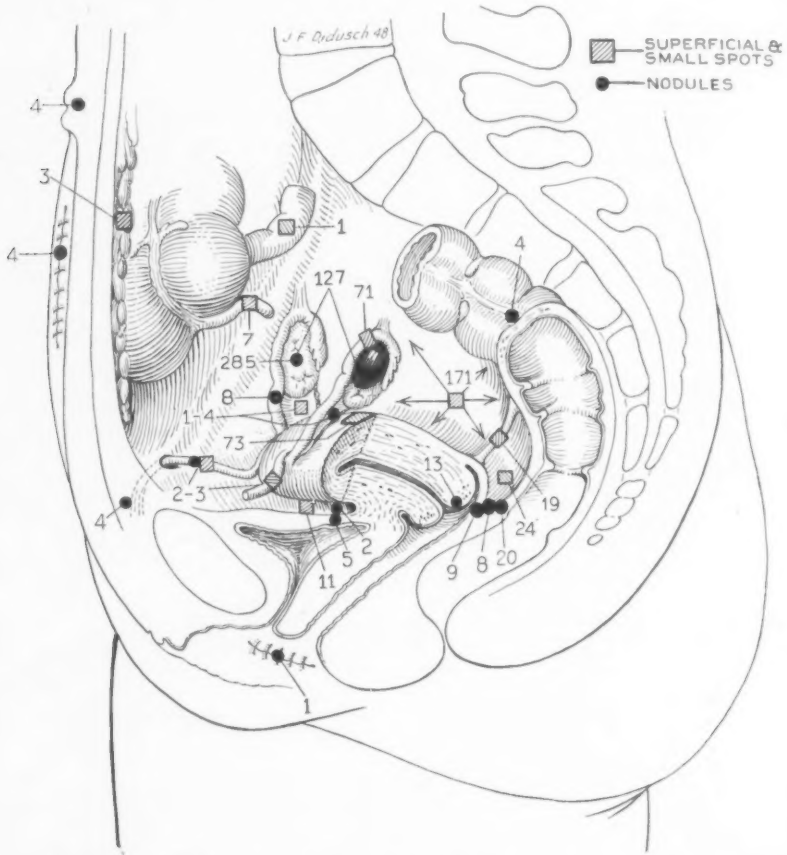


FIG. 1.—Location of external endometriosis in 516 cases. The numbers add to more than 516 because of multiple types and locations of lesions in single cases.

tiated by hormone assays. Sixty-three, or 12.2 per cent, of the cases showed adenomyomas or adenomyosis, and in this same period of 15 years there were 467 additional cases of internal endometriosis in our laboratory without evidence of external endometriosis, indicating that these two diseases are etiologically separate. Retroposition of the uterus in only 9.5 per cent of the cases is unusually low and probably not accurate, because only the deep third

degree, unequivocal ones were indexed as such. We are in agreement with Beecham[15] that there is a relationship between retroposition of the uterus and external endometriosis and that patients with these two findings usually have the most severe symptoms. There is no more important part of the conservative treatment of endometriosis than an adequate suspension of the uterus.

Microscopic diagnosis of chronic salpingitis was made in 21.7 per cent of the cases and hydrosalpinx in 3.9 per cent. The irritation from the progressive growth and intermittent leakage of the adjacent endometrial cyst is sufficient to produce a disturbed function of the tube and a microscopic picture of chronic salpingitis, but only infrequently does it produce total closure. This

TABLE X.—*Associated Pelvic Findings.*

	Number in Total Cases—517	Percent of Total Cases*
Myoma	296	57.4
Adenomyoma or adenomyosis	63	12.2
Endometrial polyp	45	8.7
Endometrial hyperplasia	13	2.5
Adenocarcinoma fundus	6	1.2
Sarcoma, uterus	4	0.8
Cervical polyp	11	2.1
Carcinoma cervix	8	1.6
Salpingitis, chronic	112	21.7
Hydrosalpinx	20	3.9
Salpingitis, acute or subacute	8	1.6
Pyosalpinx or tubo-ovarian abscess	10	1.9
Hematosalpinx	11	2.1
Salpingitis isthmica nodosa	6	1.2
Carcinoma, tube	1	0.2
Pregnancy, tube	1	0.2
Corpus luteum cyst or hematoma	68	13.2
Benign cyst or tumor, ovary	42	8.2
Malignant cyst or tumor, ovary	8	1.6
Parovarian cyst	7	1.4
Retroposition, uterus	49	9.5
Prolapse, uterus	5	1.0
Appendiceal disease	4	0.8
Pregnancy, intrauterine	3	0.6
None	120	23.3

* The total is more than 100% because of multiple lesions in many patients.

fact was a strong point in Sampson's original theory of retrograde menstruation. Rubin's tests before operation in 33 of this series of cases showed tubal patency in 25.

There were four cases of pregnancy encountered at the time of operation. One of the authors, (R.B.S.), reported two of these cases in a previous article.[16] One of these had a cesarean section and exploratory laparotomy because of a ruptured endometrial cyst when 36 weeks pregnant, and the other had a unilateral salpingo-oophorocystectomy and a resection of an endometrial cyst from the opposite ovary when 12 weeks pregnant. The latter patient subsequently delivered her child at 35 weeks, and had a second delivery of a viable child. The two additional cases did not deliver the pregnancies under consideration. The third case was a 38-year-old patient with two living children

who was operated upon because of a symptom-producing endometrial cyst of one ovary, and pelvic endometriosis. A very early, unsuspected, intrauterine gestation was discovered. The fourth case had a ruptured tubal pregnancy with a tubal nodule of endometriosis after two previous term deliveries. It was a surprise to the authors that more cases of tubal pregnancy were not found in association with external endometriosis.

HAVE ANY CASES OF EXTERNAL ENDOMETRIOSIS SHOWN A MALIGNANT TRANSFORMATION?

Students are taught and patients are reassured that endometriosis is a benign process, limited in its progression and its major symptoms by the dura-

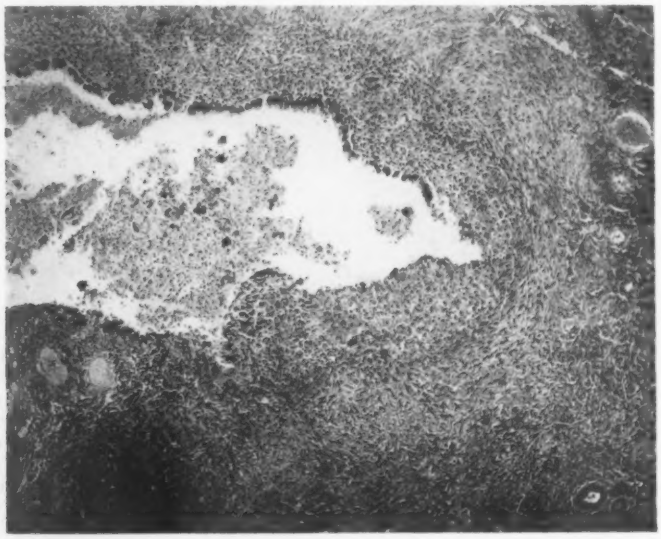


FIG. 2.—(Case 75). An area in the wall of the benign endometrial cyst of the right ovary.

tion of menstrual function. More recently this dictum is being skeptically reviewed, as in the reports of Miller, *et al.*[17] and Novak.[18] Miller, *et al.* reviewed the literature up into 1947 and concluded that their case represented the third example of adenocarcinomatous transformation in a benign endometrial cyst of the ovary. The rigid criteria established by Sampson were followed. These were: (1) the co-existence of benign and malignant tissues in the same ovary which have the same histologic relationship to each other as in carcinoma of the body of the uterus; (2) the carcinoma must actually be seen arising in the benign tissue, and not invading it from some other source; (3) additional supportive evidence includes the attendance of tissue resembling endometrial stroma about characteristic epithelial glands, and the finding of old hemorrhage rather than fresh.

In the present series eight cases of co-existing malignancy of the ovary were found. Two were epidermoid carcinomas arising in dermoid cysts and one was a small granulosa cell tumor with anaplastic change. Three were papillary serous cystadenocarcinomas with associated pelvic endometriosis in one, an endometrial cyst of the opposite ovary in the second, and ovarian endometriosis plus metastatic adenocarcinoma in the third. The two remaining cases did not fulfill the criteria for malignant transformation of an endometrial cyst, but the pathologic study created a high index of suspicion.

Case 75.—This 42-year-old white female was operated upon by Dr. Leo Brady on November 23, 1936. He did a subtotal hysterectomy and a bilateral salpingo-oophorectomy for bilateral cysts of the ovary. Microscopic study revealed a typical endometrial cyst (Fig. 2) and a corpus luteum cyst of one ovary and a partially cystic adenocarcinoma of the remaining ovary. In, and lining the thickened wall of, the malignant cyst were areas of old fibrosis and hemorrhage and the epithelium at various points was one layer thick, suggesting endometrial glandular epithelium (Figs. 3, 4 and 5). However, at no point in numerous sections could this epithelium be called perfectly benign. She received a full course of roentgen ray therapy following operation. Autopsy done two and one-half years later at the University of Virginia School of Medicine disclosed an extensive carcinomatosis peritonei.

FIG. 3

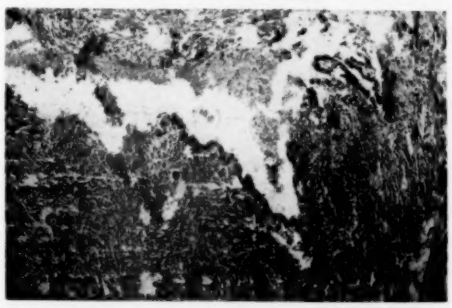


FIG. 4

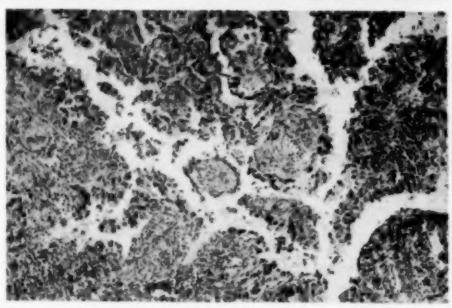


FIG. 5

FIGS. 3, 4 and 5.—(Case 75). Three areas in the wall of the malignant cyst of the left ovary. The upper and middle sections show areas in the lining and the wall, which suggest benign endometriosis. The epithelium is only one layer thick, but the nuclear changes are excessive. The lower section is definitely proliferative and malignant.

Case 515.—This 52-year-old patient had a total hysterectomy and a bilateral salpingo-oophorectomy for bilateral ovarian cysts by one of us (R. W. TeL.) on November 12, 1947. One ovary proved to have been converted into a typical endometrial cyst and the other ovary was a partially solid adenocarcinoma (Figs. 6, 7 and 8). No endometriosis could be identified in this malignant ovary but the uterine endometrium was transformed into an adenocarcinoma indistinguishable microscopically from the ovarian adenocarcinoma. Twenty-three months later she has a probable recurrence of the malignancy in the abdominal scar.

No claim is made that these cases unequivocally represent adenocarcinomatous change in a benign endo-

metriosis process. These cases and other cases in the literature give the impression that, though rare, such a transformation is possible and further confirm the teaching that any ovarian cyst, except a physiologic one, is potentially malignant.

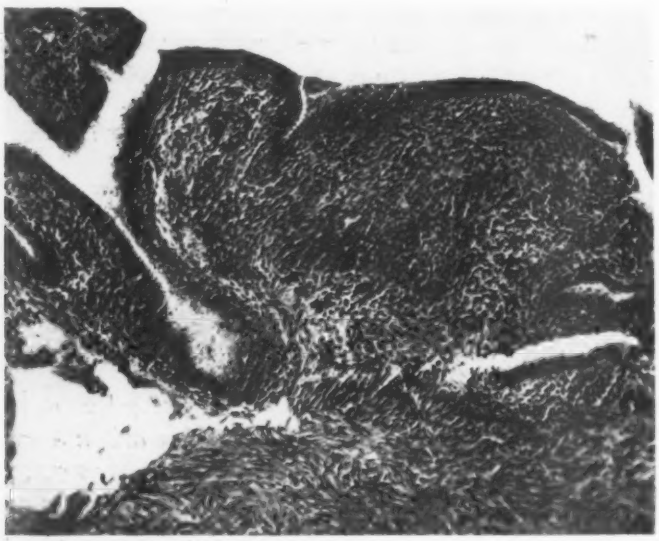


FIG. 6.—(Case 515). An area in the lining wall of the benign endometrial cyst of the right ovary.

IS PREVIOUS PELVIC SURGERY A FACTOR IN THE INITIATION, SPREAD AND GROWTH OF ENDOMETRIOSIS?

Sampson[19] felt that pelvic surgery without disturbing the endometrium could initiate endometriosis, particularly the "endosalpingiosis" type. He also considered the increasing number of pelvic examinations, uterine curettages, and Rubin's tests to be at least partially responsible for the increasing prevalence of the disease. The distribution of pelvic endometriosis makes it highly probable that showering from an endometrial cyst is responsible for much implantation, but immediate flare-up of symptoms or evidence of accidental transplantations following conservative surgery for an endometrial cyst are the exception. It is a rare endometrial cyst which can be surgically removed without rupturing.

Two hundred and ninety-two, or 56.6 per cent, of the present series had no previous major or minor gynecologic surgery and no previous appendectomy. Ninety-three or 18.1 per cent had previous major gynecologic procedures, 58, or 11.2 per cent, had previous minor gynecologic procedures only, and 73, or 14.1 per cent, had previous appendectomy only. There are no statistics available for the comparative incidence of previous operative procedures on an unselected group of gynecologic patients, but these percentages seem to the authors to be only slightly, if any, in excess of what could be considered as

normal. The relationship of accidental endometriosis, such as scar endometriosis and of cervical endometriosis, to previous operation is definite and has been discussed under location. Two interesting findings were brought to light in this particular study. Of 33 Rubin's tests done before operation in these cases, 25 had patent tubes, four had closed tubes, and in four instances the patient did not know the result of the test. Although not as formidable as Sampson's finding of 284 tubal patencies out of 293 patients with endometriosis, it does uphold the impression that usually the tubes are not closed.

FIG. 7

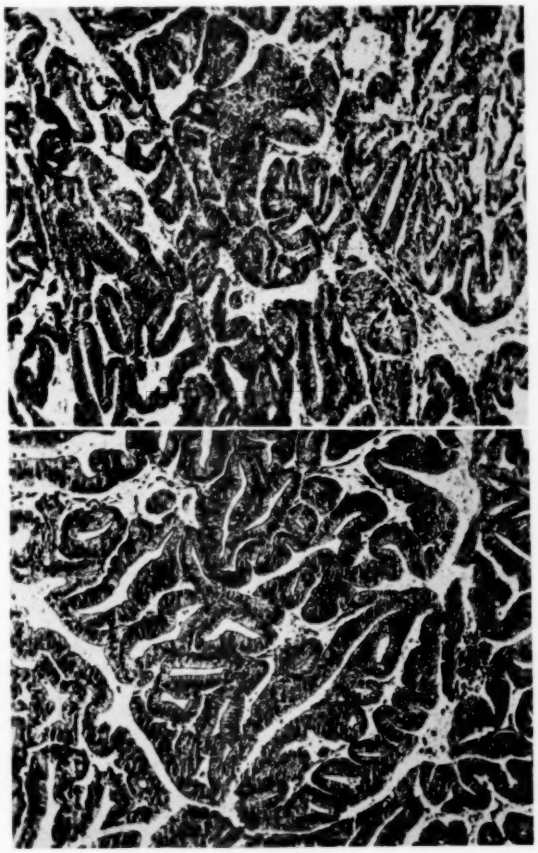


FIG. 8

FIGS. 7 and 8.—(Case 515). The upper section is from the adenocarcinoma of the body of the uterus. The lower section is from the more solid portion of the tumor of the left ovary. Microscopically these two sections are identical.

The second observation is concerned with the patients who had previous bilateral salpingectomy, unilateral salpingectomy of the remaining tube, tubal sterilization, or other procedure which terminated the utero-tubal-peritoneal pathway. There were 37 such cases who subsequently showed endometriosis. Twenty cases remain if the patients are eliminated who, from the history of or from the absence of previous pathologic study, might have had endometriosis at the preceding operation and also those who showed accidental endometriosis, such as in an abdominal scar. Eight of the 20 cases had endometriosis found two to ten years after closure of this pathway and 12 of the 20 cases had endometriosis found ten to 26 years after. Seventeen of the 20 cases were ovarian endometriosis and/or pelvic endometriosis, and none could be considered as endosalpingiosis.

Two cases are most unusual. A Russian dancer gave her age as 34 (thought to be her stage age) and the history of an operation in Russia 26 years before for peritonitis. At the time of operation in 1935 the tubes were found to have been removed at the 1909 operation and there were two large endometrial cysts

of the ovaries, the largest extending above the umbilicus and containing 2500 cc. of brownish-black liquid. A second case, 46 years of age, had a total abdominal hysterectomy at the age of 24, after three previous term pregnancies and two abortions. At the time of operation in 1944 she had 6 cm. endometrial cysts in each ovary. This group of 20 cases is another bit of suggestive evidence against the "retrograde menstruation" theory of Sampson. It is difficult to conceive of operatively undetectable endometriosis remaining dormant for such a period of time.

IS PRESERVATION OF THE CHILDBEARING FUNCTION WORTHWHILE IN THE TREATMENT OF ENDOMETRIOSIS?

In this hospital the treatment of palpable symptomatic endometriosis has been and remains almost entirely surgical. Roentgen ray castration is reserved almost exclusively for the recurrent cases with minimal pelvic masses and maximum symptoms. Testosterone, as recommended by Hirst,[20] is rarely used, and we have had no experience with the use of large doses of synthetic estrogens, as advocated by Karnaky.[21] The reasons for this preference have been on basic theoretical grounds. In the younger patient, desirous of children, the reproductive function can usually be preserved with the understanding that subsequent surgery or roentgen ray treatment may be necessary. In the fourth decade the patient can at least be allowed to retain an entire ovary or a part of an ovary, eliminating the psychic shock of premature castration. The disease process, by its very infiltrative and fibrophilic nature, usually produces symptoms of mechanical origin and a surgical approach is more rational and more certain of correction. Finally we know from previous error that it is not uncommon for a preoperative diagnosis of endometrial cyst to prove microscopically to be a malignant cyst of the ovary. Persisting ovarian enlargement beyond physiologic limits *must* be treated surgically.

The cases are divided into three groups for study. The conservative surgical cases include those in which childbearing function is preserved, the semi-conservative those who are allowed to retain ovarian tissue but anatomically unable to conceive, and the radical those who are deprived of all ovarian tissue.

Examination of Table XI-A and Table XI-B will show the type of surgery done in each age group, and comparison of the two tables will show the tendency towards less radical surgery in the two younger age groups when the principal lesion encountered is endometriosis. Each year the trend in this hospital and others, as recently stressed by Beecham,[15] and Cashman,[22] has been towards the preservation of childbearing function. The authors are still at a loss for an explanation of the preservation of one ovary in a 52-year-old patient, accounting for the 4 per cent incidence for semi-conservative procedures in this age group of Table XI-A.

Final judgment of the value of maintaining reproductive function awaits the answer to two questions. How many term pregnancies resulted? How many patients underwent subsequent surgery or roentgen ray treatment because of persistence or exacerbation of the disease process? One hundred and seven

cases in the entire group were anatomically able to conceive following operation. Twenty-four cases were eliminated from consideration because of the lack of desire for future pregnancies or because they were over the age of 42 at the time of operation here. This leaves 83 cases who could reasonably be expected to conceive and 64 of these cases have been followed from nine months to 15 years. Seven of the 19 cases not followed were single, separated or divorced at the time of operation and one case had an Estes procedure. In the 64 patients there were 38 subsequent pregnancies in 26 patients. Twenty

TABLE XI-*A*.—*Type of Surgical Treatment.*

Total Cases—516	19–30 Years Per Cent	31–40 Years Per Cent	41–50 Years Per Cent	Over 50 Years Per Cent
Conservative	58.3	17.9	5.4	4.0*
Semi-conservative	24.1	46.0	34.5	4.0
Radical	17.6	36.1	60.1	92.0

* Consists of only one case—a cervical endometriosis found upon amputating the cervix.

TABLE XI-*B*.—*Type of Surgical Treatment.*

Primarily Endometriosis Cases—243	19–30 Years Per Cent	31–40 Years Per Cent	41–50 Years Per Cent	Over 50 Years Per Cent
Conservative	74.4	35.8	18.4*	....
Semi-conservative	12.2	35.0	7.9	....
Radical	13.4	29.2	73.7	100%

* This figure is proportionately high because it includes four cases of diagnostic procedures only; three cervical biopsies and one biopsy of the rectovaginal septum, per vaginum.

patients had term deliveries; of these, seven had two term deliveries, one had three term deliveries and one abortion, one had an abortion in addition to a term delivery, and one, pregnant at operation, delivered this child six weeks prematurely and had a second premature delivery, both of which lived. Three of the 26 patients were pregnant at the last examination (ten weeks, 12 weeks and 6 months respectively), and one of these had a previous spontaneous abortion. Three of the 26 patients had a spontaneous abortion only. In summary, 26 of the 64 cases followed or 40.6 per cent conceived and at least 20 of the 64 or 31.3 per cent had term deliveries. To our knowledge, this is the highest incidence in the literature of subsequent pregnancies following conservative operation for endometriosis.

Eight of the 64 cases followed had subsequent hysterectomy or removal of the remaining pelvic organs, one had subsequent suspension and partial ovarian resection, and one had roentgen ray castration. Thus 15.6 per cent of the followed cases had another surgical procedure or roentgen ray sterilization. It appeared noteworthy to us that only three of these secondary operations were done in our clinic and one wonders whether they were all necessary. By comparing these figures with the percentage of resulting pregnancies, it is convincing evidence that preservation of the childbearing function is definitely

worthwhile, provided this is a major request of the patient and that she understands surgery or roentgen ray may be necessary at a later date. With the passage of years there may be more who need subsequent specific treatment, but there will also be more pregnancies.

IS PRESACRAL NEURECTOMY INDICATED AS AN ADJUNCT TO CONSERVATIVE SURGERY IN ENDOMETRIOSIS?

Because dysmenorrhea is a frequent complaint in endometriosis, presacral neurectomy has been advocated in those cases in which the uterus is saved. Reports indicate that freedom from menstrual pain by presacral neurectomy has been less certain when there is associated endometriosis than in primary dysmenorrhea.[23] Cooke[25] attributed this to the undisturbed sympathetic nerve supply to the preponderant ovarian lesion via the infundibulopelvic ligament and recommended division of this ligament. However, "ovarian neurectomy" has seldom been done, for, on theoretical grounds, there would be a critical impairment to the blood supply of a saved ovary.

Presacral neurectomy was done 15 times in this series. Complete relief from menstrual pain was obtained in six cases, moderate relief in three cases, and slight relief in one. In one instance the procedure was done with success in association with a hysterectomy; this patient had a painful, non-constricting rectosigmoid endometrial infiltration and the preservation of one normal ovary was especially indicated. Four patients could not be followed. From this small series it would seem advisable to do a presacral neurectomy whenever the uterus is preserved in a patient with dysmenorrhea and endometriosis.

WHEN FEASIBLE, SHOULD A NORMAL OVARY OR PART OF AN OVARY BE CONSERVED?

Of the 107 cases (not including seven diagnostic biopsies in elderly patients) conservatively treated with preservation of the childbearing function, 82 were followed for nine months to 15 years. Nine had subsequent surgical treatment, three roentgen ray castration, and one a radiation menopause by intrauterine radium. This represents an incidence of 15.9 per cent in which later definite treatment was necessary in this group, and 12.2 per cent if the three procedures which were done for incidental developments are excluded (two for large myomas and one for functional bleeding).

One hundred and eighty-six patients were surgically treated with the preservation of some ovarian tissue but with the loss of reproductive function. Ninety-eight of this group were followed. None of these had subsequent abdominal surgery, but four were given roentgen ray castration because of recurrent endometriosis. One was given roentgen ray therapy and radium for carcinoma of the cervical stump. Two cases were advised to have another operation but refused. Two died of unrelated diseases. In this group only four cases in the 98 followed or 4.1 per cent were given radical treatment because of persisting or recurrent endometriosis.

Of 216 cases treated by radical surgery 112 were followed. As might be expected, in no instance was endometriosis the reason for subsequent surgery. This group includes all of the postoperative deaths in the total series of 516 cases. There were five deaths, an operative mortality of almost one per cent. None of the deaths were in the 243 cases operated primarily because of external endometriosis. The causes of death were as follows:

1 — Sickle cell anemia and pneumonia
1 — Cardiac failure
1 — Evisceration and secondary closure
1 — Pulmonary embolus
1 — Uremia (in mild uremia preoperatively secondary to ureteral obstruction from large myomas).

Nine of these 112 cases followed died in six months to five years from the associated malignancy present at operation or from unrelated conditions.

DOES THE POSSIBILITY OF ACTIVATION OF THE ENDOMETRIOSIS PROCESS OBVIATE THE USE OF ESTROGENIC HORMONES FOR MENOPAUSAL SYMPTOMS?

From time to time the literature contains a warning, based usually on isolated case reports, against the use of estrogenic substances in any case which reveals endometriosis at operation. In the present study there is a record of 32 of these 516 cases receiving adequate dosage of a natural or synthetic estrogenic substance for the control of menopausal symptoms. In no instance was there reason to believe that the process had been activated. This agrees with Sanders.[10]

IN VIEW OF THE ASSEMBLED DATA WHAT WOULD SEEM TO BE A SOUND POLICY IN THE TREATMENT OF EXTERNAL ENDOMETRIOSIS?

Treatment of external endometriosis is dependent upon the symptoms and the palpable extent of the disease process, the age and general physical condition of the patient, the need and desire for the preservation of childbearing function and/or menstruation, and the psychosomatic evaluation of the patient. In the absence of palpable pelvic disease, exploratory laparotomy on the basis of symptoms alone is rarely indicated. Increasing use of the culdoscope as recommended by one of us (R.W.TeL.)[24] in symptomatically suspicious cases will do much to reduce the incidence of unnecessary pelvic surgery. In the patients up to 35 years of age who are sterile and desirous of having children, every effort should be made to conserve childbearing function, and operation should not be delayed until conservative surgery is no longer possible. A preoperative Rubin's test gives the surgeon useful information in planning surgery. All evident areas of endometriosis should be excised or fulgurated, the uterus suspended if necessary, and a presacral neurectomy done if dysmenorrhea is a symptom. For patients between the age

of 25 and 45 who have completed their families or who are not desirous of children, all endometrial lesions should be excised or fulgurated and, unless the patient seriously objects, the uterus should be removed. A total hysterectomy is preferable to a subtotal, but many times it is not wise in the presence of an extensive posterior cul-de-sac involvement. Unless an extensive process has destroyed practically all ovarian tissue, an ovary or part of an ovary should be conserved in this group. Patients beyond the age of 45, psychosomatically stable, should generally have all ovarian tissue and the uterus removed. If there is serious question as regards her nervous reaction to castration, some normal ovarian tissue may on occasion be left. Surgery is the principal treatment and conservative surgery the principal aim. Since the best preoperative intentions may be altered by visualization of the pelvic organs, it is the surgeon's foremost duty to the patient to make her cognizant of both the conservative aim and the radical possibilities, as well as the possible chance of recurrence if conservatism is practiced. Roentgen ray castration is usually reserved for recurrent endometriosis with the absence of a large mass or serious symptoms on an evident mechanical basis. When it is used, the diagnosis must have been established by previous surgery, for otherwise carcinoma of the ovary can never be ruled out with certainty.

There is an insufficient evidence at present to permit anyone to be dogmatic regarding the effect of stilbestrol and testosterone on endometriosis. Hence, hormonal therapy should be used only for those patients requiring treatment who refuse surgery. There appears to be no reason for withholding estrogenic substance within therapeutic limits from postoperative patients with menopausal symptoms.

CONCLUSIONS AND SUMMARY

1. Five hundred and sixteeen cases of proved external endometriosis encountered at operation in one hospital during a 15-year period from 1933 through 1947 are studied clinically and pathologically.

2. One hundred and ninety-seven additional cases were diagnosed as external endometriosis at the operating table, but these lacked pathologic proof and are not included in this study. One hundred and fifty-eight of the 516 cases in the present series were diagnosed in the laboratory alone.

3. Two hundred and forty-three of the 516 cases, or 47.1 per cent, were operated upon principally because of endometriosis.

4. External endometriosis is significantly more frequent in the higher social and economic level of society. It is encountered in 2.7 per cent of the gynecology abdominal operations in the colored female, 3.2 per cent in the white charity patient, and 15.9 per cent in the private patient.

5. The incidence is increasing from 3.2 per cent of the pelvic laparotomies in 1933 to 9 per cent of the pelvic laparotomies in 1947. This increase is almost entirely a result of the increment of 7.5 per cent to 21.8 per cent during the same period in the white private class of patients.

6. It is encountered most frequently in the period between 31 to 40 years of age; in the latter half of this decade for all cases and the first half for those cases in which endometriosis is the principal lesion.

7. The relative sterility rate was 46 per cent and the absolute sterility rate 33.5 per cent in the total group.

8. No significant conclusions could be drawn from a study of the time interval from the last pregnancy to the operative finding of endometriosis.

9. Menorrhagia and/or metrorrhagia is not a common symptom of endometriosis alone. Although a symptom in 44.1 per cent of the total cases and 26.6 per cent of the primarily endometriosis cases, it is usually due to an associated pelvic lesion.

10. Pain and dysmenorrhea are frequent symptoms, but again may just as commonly be dependent upon associated lesions. Twenty-five and three tenths per cent of the cases had increasing or acquired dysmenorrhea and 26.9 per cent had no pain or dysmenorrhea.

11. Seventy-nine and eight tenths per cent of cases revealed endometriosis or an endometrial cyst in one or both ovaries.

12. Myomas were present in 57.4 per cent of the total cases and endometrial hyperplasia in 2.5 per cent. Adenomyomas or adenomyosis was found in 63, or 12.2 per cent, of the cases. There were three intra-uterine and one ruptured tubal pregnancy encountered in this series.

13. Two cases of ovarian adenocarcinoma are briefly described as examples of possible malignant transformation of endometriosis.

14. The Rubin's tests done preoperatively were usually successful. Twenty cases that had previous surgery disrupting the utero-tubal-peritoneal pathway and no evidence of endometriosis at that time showed endometriosis two to 26 years later. This is considered a strong argument against the "retrograde menstruation" theory.

15. Surgical treatment is advocated and conservation of childbearing function or ovarian tissue is stressed.

16. Thirty-eight subsequent pregnancies in 26 patients of 64 followed was the reward for preserving childbearing function. Twenty cases had one or more term deliveries, while three were pregnant at the last examination, and three had only an abortion. Thus 40.6 per cent of the 64 conceived after operation and 31.3 per cent had term deliveries.

17. Twelve and two tenths per cent of the cases followed in the group which retained childbearing function after operation, and 4.1 per cent of those followed in the group in which ovarian tissue was spared but reproductive function not maintained, had subsequent definitive treatment in the form of surgery or roentgen ray because of symptoms of recurrent endometriosis.

18. Presacral neurectomy is considered a useful procedure when the uterus is not removed and dysmenorrhea is a major preoperative complaint.

19. In this group of cases there is no evidence that estrogenic hormones activated the endometriosis when given in therapeutic amounts for the alleviation of menopausal symptoms.

20. A treatment policy for external endometriosis is presented based upon this group of cases and recent clinical reports. Presumptive diagnosis and operation on the basis of symptoms alone is condemned. Culdoscopic examination is recommended as an additional diagnostic procedure and as a means of preventing unnecessary surgery.

The authors wish to thank the members of the visiting staff of the Department of Gynecology for the use of their private patients in this study and Mrs. Mary Linderman and Miss Mary Linderman for their faithful assistance in compiling the statistical data.

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DISCUSSION.—DR. JOE V. MEIGS, Boston: You have heard a very wonderful exposition of this entity. Doctor TeLinde and I agree almost 100 per cent. I discussed this subject before you two years ago when I was first a member and the Association met at Hollywood, Florida. Then I brought out a question which I think is very pertinent, the age of marriage and the frequency of childbearing. I have been accused by the New York Times of practicing outmoded eugenics; I have been cheered by the Catholic newspaper of Los Angeles; I have been disturbed by a letter from the Protestant group in Los Angeles; and the Consumers' Digest accused me of starting class warfare. I really feel, however, that from Doctor TeLinde's figures and from my own (if I may show these slides) that there is a difference between the private and public ward cases, and that we, as doctors and as individuals of intelligence, who have enough money to help our children have babies, should do so.

These figures show in our two series of private patients, one in 1941 and one in 1948, that of 400 consecutive abdominal operations the incidence of endometriosis in the private group was 28 per cent and 30 per cent—pretty comparable figures. In the Massachusetts General Hospital the figures show 5 per cent and 5.75 per cent incidence in a like number of patients. In other words, it looks as though there were a rather stable state of affairs.

Those of us who can afford to have children put off the day of marriage and avoid having children; therefore I have advocated early marriage and early childbearing among our people, but consider figures that have recently come out on a large study of patients with cancer of the cervix, a disease much more important than endometriosis. Dr. Herbert Lombard, of the State Department of Public Health in Massachusetts, is an excellent statistician (slide) and his figures show—and this, I think, is very important—that 45 per cent of the patients with cancer of the cervix were married below the age of 20; only 16 per cent of patients with cancer of the breast were married below the age of 20; and 18 per cent of the general population. This figure is constant; it is not a question of how many children you have or how you space your children or anything else; it is the question of marriage before the age of 20. A statistician from New Orleans has been reviewing the hospital records there, and finds in Louisiana—where marriage takes place earlier than in the North—that 60 per cent of cancer of the cervix develops in women married before the age of 20. This was brought out in "grand rounds" in our hospital not long ago, and Dr. Edward D. Churchill said "Doctor Meigs now finds himself on the horns of a dilemma"—and I am. First we advocate our children marrying early and having children, then we turn around and find figures like this that give us cause to think hard about the situation.

DR. JOHN C. BURCH, Nashville, Tenn.: It is a pleasure for me to discuss a paper by Doctor TeLinde, one of the masters in the field of pelvic surgery. My first point is that Doctor TeLinde reminds us that many cases of endometriosis are removed by the general surgeon as carcinoma. The converse is quite true; many cases of carcinoma are not removed by the obstetrician and gynecologist. The point is that any man who goes into the abdomen must be able to cope with any situation he meets therein. Endometriosis, as Doctor TeLinde stated, is often asymptomatic, and our range of error in diagnosis is not so great as to permit conservative treatment in selected cases.

However, we are oftentimes faced with a situation in which we have a case in which endometriosis is suspected, but we cannot exclude other conditions which may be malig-

nant or may later become malignant, and operation is indicated. In such a situation the surgeon is often faced with a difficult problem. I recall such an instance not long ago in which I was called upon to see a young woman who had an ovarian cyst. I could make out no signs of endometriosis. She was 22 years old, and was engaged to be married in September; I saw her in July. I found a condition exactly like that shown in the beautiful colored slide by Doctor TeLinde, except that the right ovary was involved to a lesser degree than in his specimen. What was my decision? To back out, to do nothing, or to do a clean sweep? I found I was in a difficult spot. The girl was menstruating regularly, she was having no pain. In spite of the fact that the ovaries appeared to be destroyed, there was obvious evidence that they had good function, as shown by the normal regular menstruation. I simply evacuated the cyst, drained out the chocolate fluid, closed the abdomen. The patient got along very well, had a smooth convalescence, was married in September, and by the following September had delivered a fine baby boy.

We can be more conservative, I think, in these young women, in the conservation of reproductive function. In the older patients I think we must approach it from an individualized standpoint, according to pelvic function. We must do the best we can for them under the circumstances.

DR. R. W. TeLINDE, Baltimore (closing): I only want to thank Doctor Burch for supporting our ideas regarding conservatism. I am sure that Doctor Meigs agrees with this point of view. We have all been amazed at times at the women who have had babies after conservative operations for extensive endometriosis. I recall one patient upon whom I operated during pregnancy. I removed all of one ovary and half of the other. She not only went through that pregnancy but has had two babies since.

I also want to add to Joe Meigs' troubles. Some time ago I received a communication from the Professor of Gynecology at the University of Quebec. He is in a unique position in that he has been gynecologist to several nunneries in the city and province of Quebec. It occurred to him that he had never seen a nun with carcinoma of the cervix. He investigated and found no recorded deaths of nuns from carcinoma of the cervix, whereas in the same convents there were 12 recorded deaths of carcinoma of the corpus uteri. In the general population carcinoma of the cervix is eight times as frequent as carcinoma of the corpus. So there should have been approximately 96 cases of cervical cancer if the occurrence of cervical cancer were as frequent as in the general population. The incidence of cervicitis in nuns is probably lower than in any other group of women, inasmuch as they are not exposed to Neisserian infection or non-specific infection resulting from childbirth. This supports the idea that irritation from inflammation of the cervix is an important factor in the etiology of cervical cancer. Now Doctor Meigs tells us that early marriage predisposes to cervical cancer and late marriage or spinsterhood predisposes to endometriosis. He has placed himself in a dilemma as to whether to subsidize his daughters to permit early marriage and childbearing, thus preventing endometriosis, or to place them in a convent and prevent cervical cancer.

WRY-NECK FACIAL DISTORTION PREVENTED BY RESECTION OF FIBROSED STERNOMASTOID MUSCLE IN INFANCY AND CHILDHOOD*

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THE DEFORMITY of congenital wry-neck may be prevented by early excision of the sternomastoid muscle that has been replaced by scar tissue, and this may be the only operation that is adequate in severe lesions (Figs. 1-9). Mikulicz recommended this in 1895, but since then it seems to have been largely forgotten and there has been enthusiasm over operations that have seemed more simple, but which often have not proved adequate.

The operation of excision preferably should be done before deformity becomes permanent, with its distortion of the facial bones. Therefore it is best done in young babies (Figs. 1-5). Just a few days in the hospital are required and no special postoperative care is necessary. Braces, collars, large collective plaster casts, postoperative manipulations, stretchings, and exercises have been recommended following other operations, but these are not needed when the fibrotic muscle has been removed.

Movements of the head in all directions in these babies are normal just after the operation and remain so. The slant-wise deformity of the face begins improving as soon as the pull is taken off the mastoid in younger children.

The uncorrected, or partially corrected, lesion is productive of such gross deformity and marked facial asymmetry that it seems worthwhile to rely only upon measures which are definitive and adequate enough to relieve it completely.

PATHOGENESIS

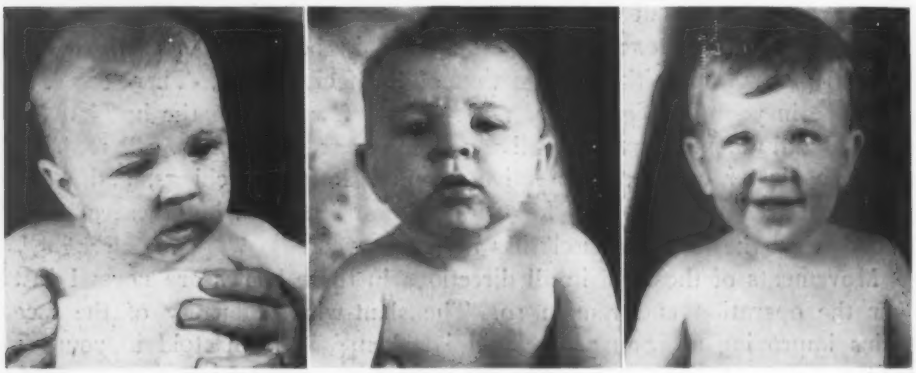
The lesion is possibly due to excessive stretching or tearing of the sternomastoid muscle during delivery, and many of the patients have a history of breech delivery. It is evident that great leverage may be exerted upon the neck, in this type of delivery, in rotating the shoulders and bringing them down, and also in trying to disengage the after-coming head from the birth canal after the body is born. Further evidence of this leverage and force is indicated by two patients who had fractured clavicles and one that had a sterno-clavicular separation. No one, however, can find criticism of the obstetrician in these difficult situations, in view of the fact that he must deliver the aftercoming head within eight minutes after the birth of the umbilicus if the baby is to live. Conversely, it is probable that some of these

* Read before the Southern Surgical Association, Hot Springs, Virginia, December 6, 1949.

children would have been stillborn if the obstetrician had been less active or skillful.

The few writers in the past who have questioned the above etiologic explanation have usually referred to children delivered by cesarean section who had the deformity. When traced to their ultimate source, these references usually involve one dead fetus (of four months gestation) described by Volcker in the German literature, and one dead fetus described by Rossi in the Italian literature. The fetus described by Volcker had been in a museum jar for 16 years when he wrote his article. Other explanations of the lesion, such as prenatal position, also have been suggested.

The first significant finding in these children is a hard tumor mass in the sternomastoid muscle which appears in the first two weeks of life (Fig. 2). This mass progressively enlarges for several weeks, and the head becomes



A B C

FIG. 1. (A, B and C)—Typical lump in neck and persistent deformity, relieved by early operation, with normal final appearance and function, at two and 14 months postoperative.

pulled over the mass, then the mass often decreases in size for several weeks and may disappear entirely. In those patients in whom the mass reaches considerable size, or remains for a fairly long time, the muscle is usually permanently shortened and inelastic. Other patients with lesser tumor masses of shorter duration may recover sufficient elasticity in the muscle and the head spontaneously straightens up. Occasional patients are seen in whom there is no history of a tumor, the pull on the head being the first thing noticed.

It has been considered formerly that the tumor represented a hematoma, but it has not been possible to find any reported patient in which this has been proved. On the other hand, there is considerable evidence against it. These patients rarely show any ecchymosis over the area. Babies who do have ecchymosis over the area usually do not develop torticollis. One of our patients had repeated aspirations of the mass at the age of 24 days without any blood being obtained, and the operator felt that the needle was in solid

hard tissue every place. Other such instances have been reported. In two of our patients who had the muscle removed at the ages of 34 days and two months, respectively (because of the rapidly increasing size of the mass and extreme deformity), the masses were composed of solid fibrous tissue with no evidence of old blood, and no hemosiderin was found on iron stains. Chandler and Altenberg[3] report similar findings of no old blood or hemosiderin in muscles removed from patients three weeks, five weeks, and six weeks of age.

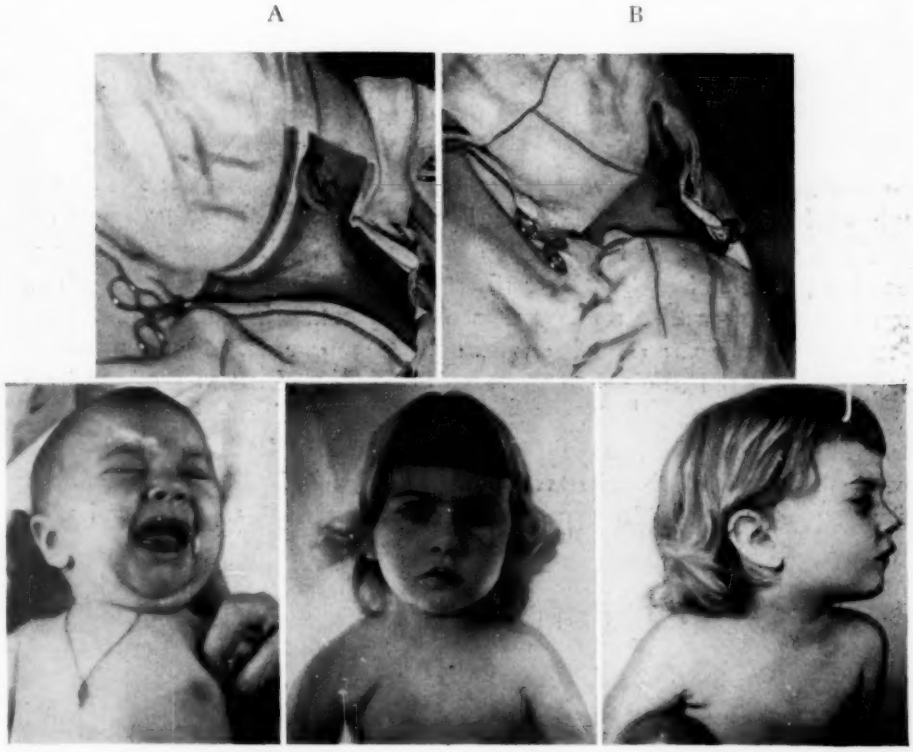


FIG. 2. (A and B)—Position for operation, lump apparent, deformity considered persistent. Short collar incision closed.
(C, D and E)—Deformity persistent in infant. Result 18 months later with normal appearance and function.

It is possible that extreme stretching of the muscle in these newborns produces a necrosis of the muscle cells, without gross hemorrhage, and that the fibroblastic replacement is an attempt at repair, rather than a true new growth (as suggested by some).

The scar replacement within the sternomastoid muscle usually extends from the clavicle to the skull; it may be partial or complete throughout, or may be complete in the lower segment and partial above. Even partial

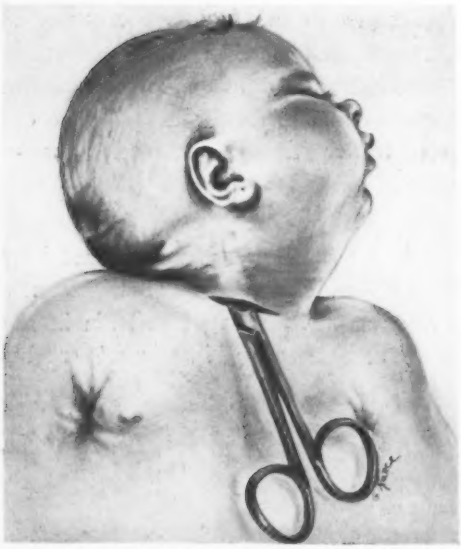
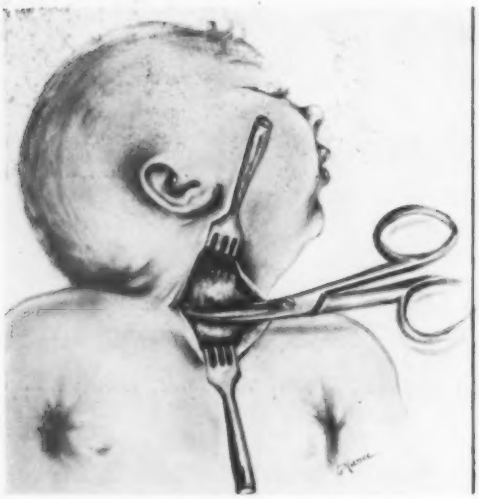


FIG. 3.—Short collar incision freeing of skin and platysma flap. Preservation of sensor and motor nerves to face.



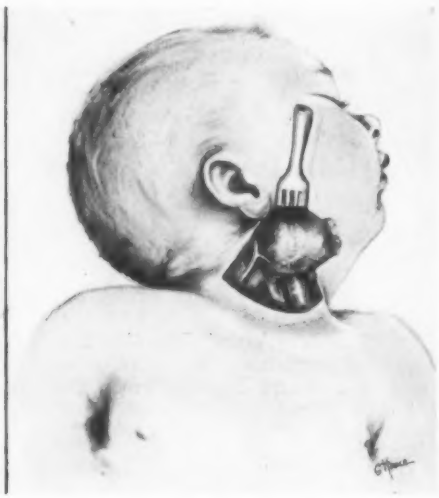


FIG. 4 FIG. 5

FIG. 4.—Careful separation of mass and fibrosed muscle from underlying structures, notably internal jugular vein.

FIG. 5.—Resection of practically whole fibrosed muscle and mass with preservation of eleventh nerve.

replacement by scar may result in marked shortening and complete loss of elasticity throughout the muscle—each little scar band acting as an individual bridle and being as inelastic as though it were a fine wire extending the length of the muscle.

At operation the muscle may be seen completely replaced by scar and will appear white on gross inspection. Others will have a fusiform, swollen, nodule of scar occupying the lower half of the muscle, so that the muscle may appear white below and red above. Even though the upper part of the

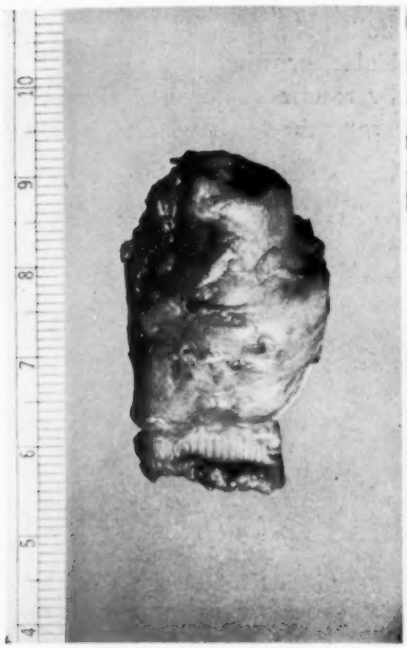


FIG. 6

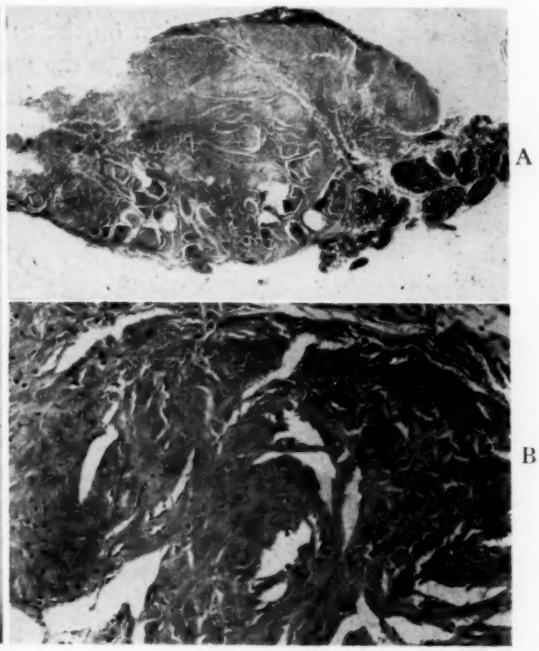


FIG. 7

FIG. 6.—Gross specimen from infant of entire mass and practically all of the fibrosed muscle.

FIG. 7. (A and B)—Photomicrographs high and low power of fibrosed mass. Extremely few muscle bundles are seen because of practically complete replacement by fibrous tissue. (Massons stain.)

muscle may look grossly normal in some of these, microscopic sections stained to differentiate muscle and fibrous tissue will usually show the fibrous tissue to predominate (Fig. 6).

Some short muscles appear uniformly red and look fairly normal throughout. However, upon cutting across them there is the sensation of cutting through tough adhesions rather than through soft muscle. On microscopic sections, they are composed mostly of scar with a sprinkling of muscle fibers which produce the red color and somewhat normal appearance (Fig. 7).

There may be adhesions between the muscle and the skin or between the muscle and the deeper structures. Because of this tenotomies will not

suffice and if they are attempted the surgeon may find himself stripping part of the muscle up from the underlying bed, or separating it from the skin, or excising the lower part of it in severe involvements in order even to get the head straight while the patient is on the operating table.

The wry-neck deformity is produced by this short, tight, bridle of scar located in the space normally occupied by the sternomastoid muscle. Movements of the head are held within the limits allowed by this bridle, but the latter is too short to allow the head to be held straight. The repeated efforts of the patient to hold his head straight result in repeated pulls and more or less constant downward tension on the mastoid process during the growing period. This force is transmitted to the moldable, growing bones of the face and skull on the affected side, and gradually results in diagonal elongation of the face and head, from the mastoid process to the top of the head on the

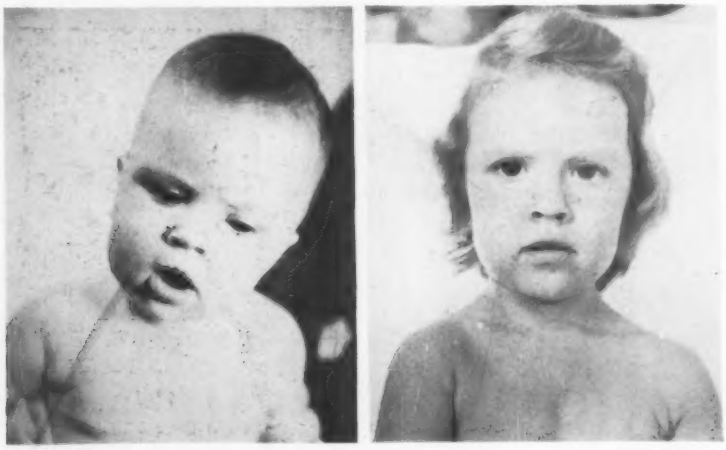


FIG. 8. (A and B)—Typical persistent and progressive deformity in infant with distortion of head, face and neck developing. Relieved by resection of muscle and normal appearance and function shown 16 months later.

normal side. Even the ear and eye on the affected side may be pulled down to a lower level, and this severe slant-wise deformity of the fact has been termed "facial scoliosis."

DIFFERENTIAL DIAGNOSIS

Wry-neck must be differentiated from *spastic torticollis* of neurogenic origin and spasm of the neck muscles from a local inflammatory lesion (*e.g.*, acute lymphadenitis or an infected branchial cleft cyst). The history that it has been constantly present since shortly after birth, together with the findings that the tightness is limited to the sternomastoid muscle, and that neck movements are normal within the limits imposed by the scar bridle, usually suffice. Common wry-neck is painless.

Cervical spine lesions (fractures, dislocations, congenital anomalies, and tuberculosis) are differentiated by history, examination, and roentgen ray findings.

BEST AGE FOR OPERATION

If the tension and pull on the head is completely released by surgery, the head position will immediately become straight, but the head and face will still be asymmetrical. If the operation is done during the growing period of a child, this asymmetry will gradually become less by the laying down of more bone on one side, and less bone on the other side, in accordance with Wolff's law. Since the rate of facial growth is most rapid during the early

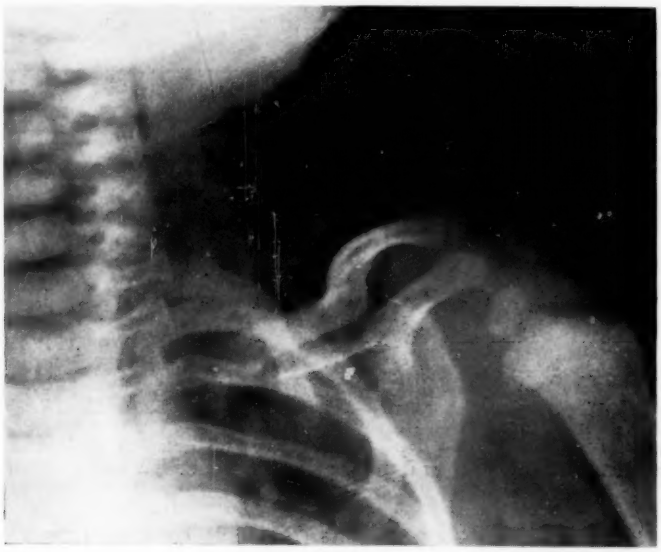


FIG. 9.—Fractured clavicle in patient with wry neck.

months and years, the earlier in life operation is done, the greater will be the eventual correction of this asymmetry. Early operation allows the face to straighten up and prevents the occurrence of severe distortion.

However, operation is not advised in all new-born babies with tilted heads. In many of these, the stretch injury has been slight with little actual necrosis of muscle fibers, but with a transient protective spasm of the muscle. These patients often recover spontaneously within a few weeks or months, and improvement is apparent early. Others with minimal necrosis of the muscle may have early spasm, with a little residual scarring that will gradually stretch out enough; improvement will be apparent within two or three months, and if mild, they can be followed for a few months longer to see if they will stretch out enough (Figs. 10, 11).

In the severe wry-neck, the stretch necrosis is so widespread that little spasm is possible and the head position may appear fairly normal during the first few days. Often the first thing noticed is the appearance of the tumor between one and two weeks of age, usually found by the mother after they are home from the hospital. This lump increases in size for a few weeks, during which the deformity gets worse; then the tumor gradually subsides, during which time the deformity gets still worse. Whenever it is apparent that the distortion is getting worse operation should be considered without waiting for further deformity.

In evaluating the milder cases, it should be pointed out that the flattening of one side of the back of the head gets worse until the child can sit up, and then spontaneously improves even though the muscle pull is no less. This improvement in the head shape after the child is sitting up is often mistaken by the parents for improvement in the underlying condition.

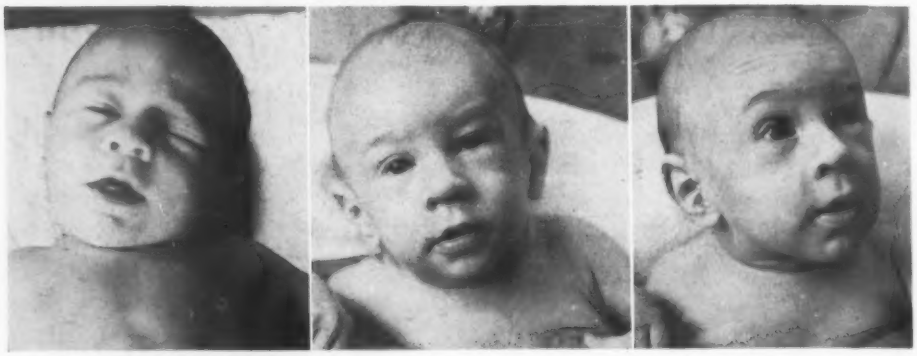


FIG. 10. (A, B and C)—Typical deformity and mass in neck, but with good enough softening and return to normal appearance and function to omit operation.

EVALUATION OF COMPLETE EXCISION OF THE MUSCLE

About the only objection to complete excision is the loss of the prominence of the anterior border and sternal head. This varies in normal individuals with the state of nutrition, being only slightly visible in well-nourished or obese patients, and more visible in undernourished individuals. It is, of course, over-prominent to the point of deformity in patients with uncorrected, or partially corrected, wry-necks.

In any event, one must balance the effect of this possible slight change in the appearance of the neck with the severe lop-sided face deformity that may occur in uncorrected, or partially corrected lesions. Plastic surgeons are especially conscious of this latter deformity, as there is very little that can be done for it in the older child or adult (Figs. 1, 2, 8, 12, 13).

Early, complete release of tension will do most to correct, prevent, or minimize this "facial scoliosis." Just releasing the tension enough so that the child can hold his head up with some effort is not enough; it should be

free and loose enough that he can turn or tilt his head into any normal position without undue effort.

Historically, Dieffenbach and others performed open tenotomy during the early part of the last century. Mikulicz[4] (of Breslau) recognized the inadequacies of this, and reported a series of patients upon whom he did complete excision of the muscle in 1895. This was taken up by some others but never became popular, because most surgeons found themselves in unfamiliar sur-

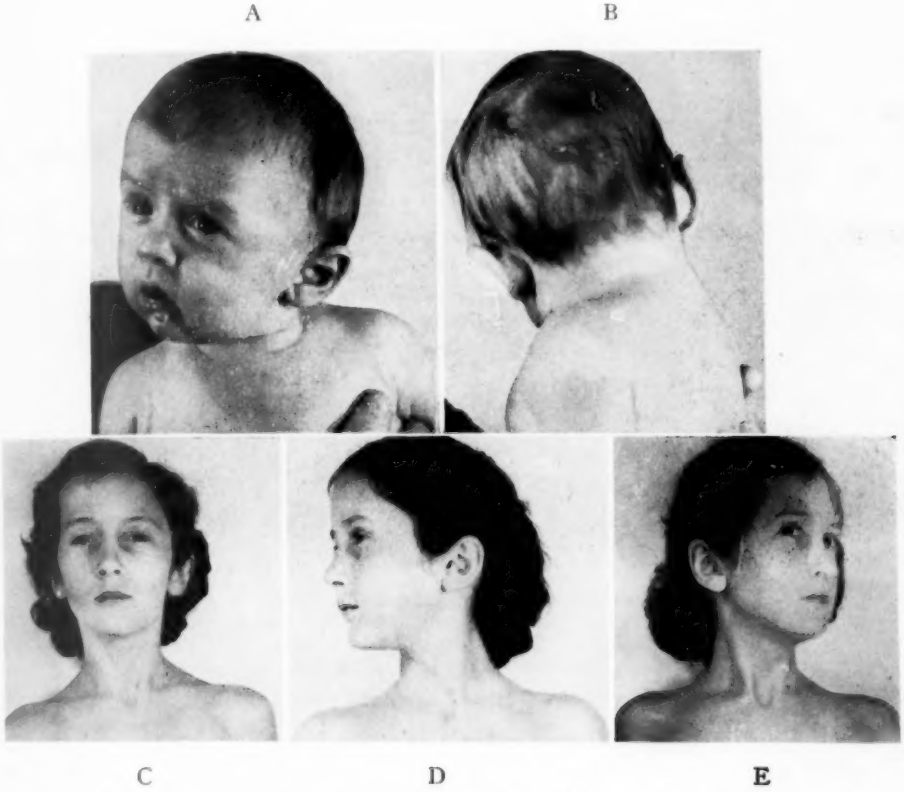


FIG. 11. (A, B, C, D and E)—Marked deformity in early infancy, but with evidence of softening and return to normal to omit operation. Normal contour and function ten years later, with slight tightness of muscle noted on close observation.

roundings when trying to dissect throughout the full length of the lateral side of the neck. About the turn of the century, subcutaneous blind tenotomy was popularized by Lorenz and Joachimstal in Vienna. It must have seemed a very simple procedure, as they demonstrated it upon adults sitting up, under local anesthesia—and many people tried it. After the dangers became apparent, it was abandoned in most places and the work reverted to open tenotomy, this time supplemented by corrective plaster casts, braces, collars, postoperative stretchings, etc., in attempts to make the operation sufficient and to

prevent recurrences. This situation has remained the *modus operandi* in many places, and repeated operations for recurrent deformity have been known in severe lesions. However, complete excision of the muscle has been the usual policy on our service for over 20 years, and Chandler and Altenberg[3] reported a large series of these in 1944.

Other procedures which have been sporadically tried have been tenotomy at both ends, and muscle-lengthening operations (which have really been scar-lengthening operations). None of these release the adhesions between the muscle and surrounding structures, nor do they correct any shortening in the cervical fascia or underlying structures. After tenotomy, healing is by pro-

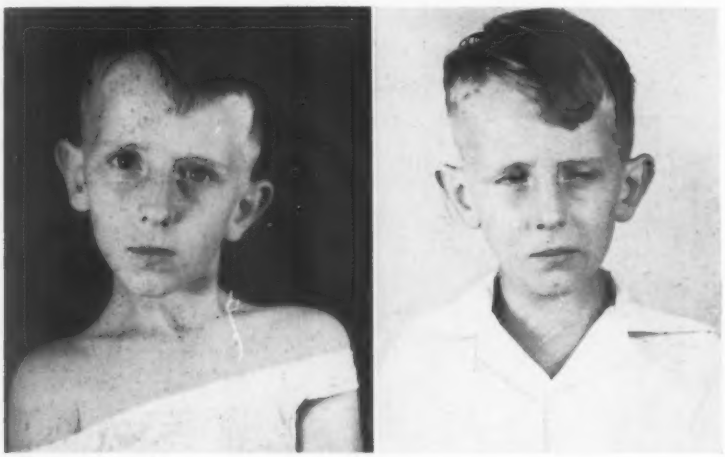


FIG. 12.—Marked deformity and distortion of face and tight fibrous mass persisting in child in whom early operation apparently had not been considered. Later correction in childhood with improvement in contour before bones have become permanently distorted.

liferation of fibroblasts from the "muscle" end to the clavicle, which later contracts down into scar with the possibility of reproducing the deformity.

Objections to removing the muscle on the grounds of function are not valid—the "muscle" is simply a non-functioning scar bridle. Even complete removal of a normal muscle (as in neck dissections for cancer) does not result in noticeable lack of function in moving the head (Figs. 1, 2, 8, 9, 12, 13).

Removal of the muscle entails more operative work than simple tenotomy, but is not difficult for anyone who is used to operating in this area. The postoperative course is short, postoperative care is minimal, and it removes the pull of the scar bridle on the face and head. The value of this in correcting or preventing facial deformity would seem to outweigh any of the objections which might be mentioned.

OPERATION

In young babies, light anesthesia is maintained with an ether vapor blower in front of the face. Endotracheal anesthesia is used in older children.

The head is turned toward the opposite side and a short collar incision of about two inches is made just above the clavicle and about parallel to the first rib. This is carried through the platysma down to the sternomastoid, and the external jugular vein is ligated and divided at the posterior border of the muscle if necessary. Dissection is carried upward on the surface of the muscle to the mastoid process (this distance is only about two inches in babies with a shortened muscle); the upper skin flap can be readily retracted enough

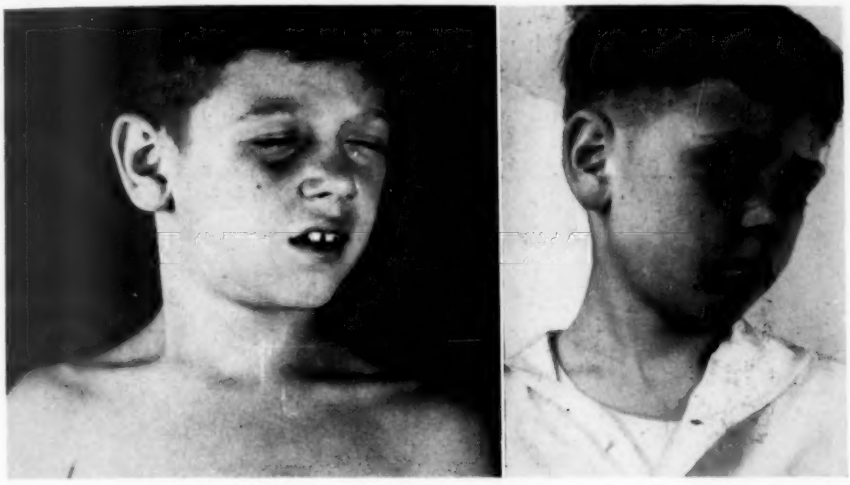


FIG. 13.—Persistent tightness and distortion in later childhood where early operation had not been done. Clavicle is elevated somewhat. Evidence that tightness may persist in part of muscle and that limited operation may be considered if this occurs. Sternal head left in this patient.

for good exposure, particularly if the head is lifted up to bring the mastoid down into the wound (Figs. 2 and 3).

Dissection is carried around the anterior border of the lower end of the muscle, and cautiously underneath the muscle until the internal jugular vein, common carotid artery, and vagus nerve are identified and separated from the muscle. The lower end of the muscle is then divided at the clavicle and sternum; a clamp is attached to it and given to an assistant to make gentle upward traction on the muscle. Dissection is carried upward beneath the muscle, separating it from the jugular, carotid, vagus, cervical fascia, and scaleni muscles. The phrenic nerve is observed overlying the anterior scalenus muscle (Fig. 4).

At about the level of the hyoid, the main trunk of the eleventh nerve emerges from underneath the posterior border of the muscle, passing obliquely

downward and backward to supply the trapezius. At this same level, or a little above, the eleventh gives off a branch to the underside of the sternomastoid. This branch is now severed, and the trunk of the nerve above is carefully freed from the underside of the muscle. The twelfth nerve will be seen near the carotid sheath above the hyoid, but is seldom adherent to the muscle. The dissection is carried on up beneath the muscle to the mastoid, and it is then cut loose from the mastoid and removed (Fig. 5).

Following this, it should be possible to overcorrect the head position without tension. If there is any tightness, one palpates along the whole side of the neck and divides any tight bands; these are usually in the cervical fascia, but may be within any of the scaleni muscles or in the anterior border of the trapezius.

After being certain that hemostasis has been secured (with 000 silk ligatures), a small rubber drain is placed along the muscle bed and the wound closed with subcuticular and surface 000 silk sutures, interrupted, and put

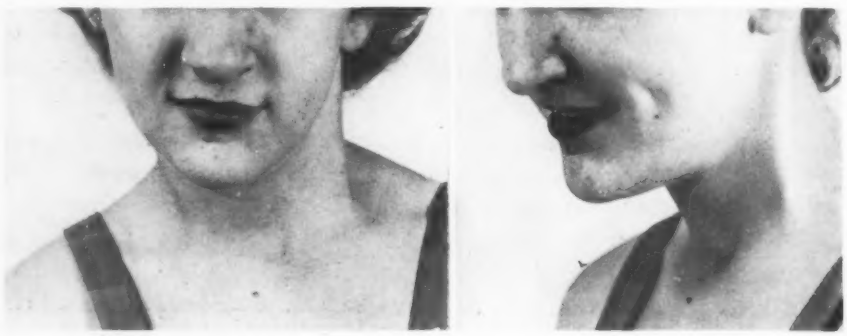


FIG. 14.—Evidence of development of tightness and distortion developing late in childhood. Noted first at 15 years in doctor's child. Probably existed throughout childhood unnoticed. Relieved by resection of the tight part of the muscle.

in close to the margins. The stitches are covered with grease gauze, and a small pressure dressing is applied with surgical waste and a strip or two of Elastoplast (Fig. 2).

The child is usually discharged from the hospital in two or three days, at which time the drain is removed. The skin sutures are removed a few days later. No postoperative stretchings or exercises, or appliances are used—and recurrence of the deformity is almost impossible. The children are examined annually for a few years as a matter of surgical interest, but no further treatment is necessary.

If one or the other muscle head, sternal or clavicular, seems to be the entire shortening element, later in childhood, partial resection of the tight head may be considered (Figs. 13 and 14).

Summary and conclusion are included in the first four paragraphs.

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DISCUSSION.—DR. O. P. HAMPTON, JR., St. Louis: Doctor Brown's paper, as his papers are always, is interesting and informative. The problem with this condition, which is seen in the necks of small children, has not been generally solved by the method he has recommended. In fact, early excision of the tumefaction is rather rare. Usually, operation is postponed until the child is several years of age, by which time the facial asymmetry may be quite disfiguring. Chandler, as Doctor Brown mentioned, has advocated early excision in an effort to prevent development of progressive deformity. Recently, Chandler has also suggested that the tumefaction may be a true tumor formation. Other concepts of the underlying pathology include not only damage at birth to the sternocleidomastoid with resulting hemorrhage and fibrosis, but also the possibility that it may be an ischemic fibrosis. (Slides)

This slide shows a case in which it certainly seemed logical to proceed with early resection to avoid severe facial asymmetry. This child was first seen at the age of four months. The photograph in the first slide was furnished by the parents at the age of five weeks. Already the deformity in the facies can be seen, the child's chin is tilted to the left and cannot be rotated any further to the right. The deformity was even more marked just prior to operation.

Doctor Brown stated that resorting to plaster fixation is not necessary, but an orthopedic surgeon never overlooks an opportunity to throw a little plaster, so after resection of the tumefaction somewhat according to the technic he mentioned, plaster immobilization was maintained for four weeks. This would seem to be a safeguard against partial recurrence.

The next slide shows the child three months after operation. The head can be rotated completely to the right. Certainly there is no deformity of the facies at this time and none has developed since.

The last slide shows a photomicrograph, showing some muscle fibers and considerable fibrosis. This, as I said, was resected at the age of four months. There is no evidence of residual blood pigment, but I am not certain there would be if it were the result of hemorrhage at birth. There is nothing to indicate true tumor formation. Perhaps it is ischemic fibrosis.

DR. JAMES BARRETT BROWN, St. Louis (closing): We could not put a satisfactory cast on one of these little babies and feel free of possible trouble from it, and we would not try to. The casts are not needed so far as we can see. The infants and children leave the hospital about the fourth day, and nothing further than a simple pressure fixation dressing is necessary. As mentioned, we do not think that casts, braces, manipulations or attempted stretching are necessary if the pull is removed at operation so that it does not recur.

THE CLOSED TREATMENT OF ACUTE HEMATOGENOUS OSTEOMYELITIS

RESULTS IN 67 CASES*

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IN 1943 FLOREY AND FLOREY[4] predicted that acute hematogenous osteomyelitis, properly treated with penicillin, probably would not require surgical intervention. Since then there have appeared in the literature numerous reports of such treatment confirming this prediction. Several investigators[1-3, 5, 6, 8, 9] have reported series of cases in which the response to penicillin therapy was good when the condition was diagnosed early and treated with adequate amounts of the drug over a sufficient length of time. However, there is some difference of opinion among these authors regarding the best treatment for abscesses, which sometimes develop even when sufficient doses of penicillin are given. The results of 67 cases of patients with acute hematogenous osteomyelitis, treated with penicillin and the usual supportive measures but no surgical drainage, were analyzed in an attempt to evaluate such treatment. They form the basis of this report.

From January, 1945, to January, 1949, there were 94 patients with acute hematogenous osteomyelitis treated by this method at Charity Hospital of Louisiana in New Orleans, Lafayette Charity Hospital, and three other hospitals in or adjacent to New Orleans, with no deaths. Follow-up data were obtained on 67 of these patients with infections caused by penicillin-sensitive organisms and treated by this method. Fairly uniform treatment was carried out in all the patients. This consisted in the intramuscular administration of 30,000 to 50,000 units of penicillin every three to four hours and aspiration of local abscesses with instillation of penicillin solution into the aspirated cavity every 24 to 48 hours, as outlined by Altemeier and Helmsworth[2] in 1945.

Local aspiration of abscess cavities is an important step in this method. It accomplishes three objectives: (1) the causative organism is identified and evaluated as to penicillin-sensitivity; (2) the pressure within the abscess is decreased; and (3) the local concentration of penicillin can be immediately raised to effective levels.

Penicillin administered systemically in sufficient concentrations sterilizes the blood stream, and if given early, may prevent actual development of abscesses and necrosis in bone. However, if abscesses develop within the bone, thrombosis of adjacent arterioles rapidly occurs;[7] this, coupled with severe local edema, results in spread of the local abscess and extensive

* Read before the Southern Surgical Association, Hot Springs, Virginia, December 6, 1949.

necrosis of bone. This necrotic abscess containing bacteria and cellular debris is in large measure walled off from the circulating blood. According to accepted surgical principles, if sufficient exudate accumulates to produce a fluctuant swelling, it should be incised and the wound left open to drain and heal by granulation. However, this exposes the wound and bone to secondary

FIG. 1

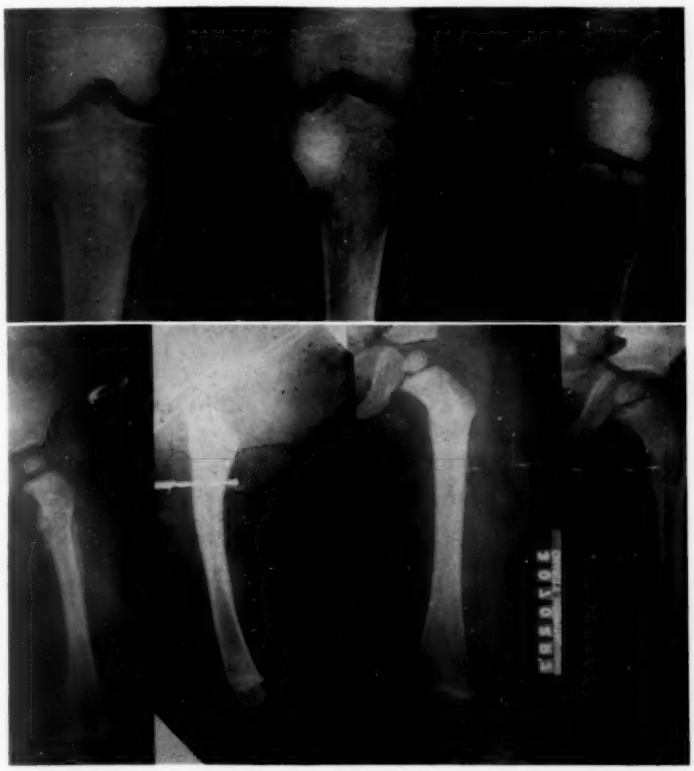

FIG. 2

FIG. 1.—Excellent result showing complete restoration of normal bone architecture in D. H., white male, age 17 years. Roentgenograms, reading from left to right, taken August 4, 1946, September 28, 1946 and February 7, 1949.

FIG. 2.—Excellent result showing minimal sclerosis or thickening of trabeculae and complete healing of osteomyelitis and pathologic fracture in F. W. R., Negro boy, age 11 months. Roentgenograms taken July 6, 1945, September 10, 1945, February 14, 1946 and November 3, 1947.

bacterial invaders which are frequently responsible for the well known chronicity and recurrences of osteomyelitis. Since it is possible to control the systemic infection by administration of penicillin, it seems preferable to avoid introduction of secondary invaders by aspirating most of the pus from the

abscess and instilling a solution of penicillin into the cavity; thus a concentration of penicillin in the abscess cavity can be obtained which is high enough to combat the bacteria that are walled off from the general blood stream. Systemic administration of penicillin, combined with aspiration of abscesses when they occur and instillation of a solution of penicillin into the abscess

FIG. 3

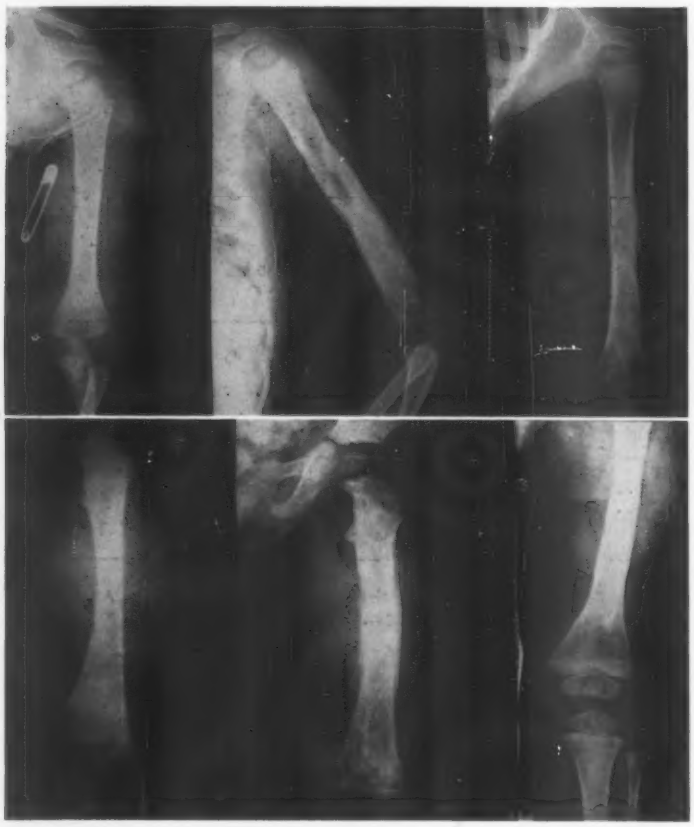

FIG. 4

FIG. 3.—Good result, showing persistent sclerosis of diaphysis, in F. K., Negro boy, age 14 months. Roentgenograms taken March 3, 1947, December 7, 1947 and November 6, 1948.

FIG. 4.—Good result, showing persistent sclerosis and overgrowth of femur length, three-fourth inch, in R. S., Negro boy, age two years. Roentgenograms taken January 12, 1947, March 8, 1947 and September 12, 1948.

cavity, has been designated as a closed method of treatment as distinguished from the open method of surgical drainage of the localized abscesses. It should be understood that this closed method of treatment in no way minimizes the necessity for routinely employing general supportive measures,

such as sedation, restoration and maintenance of blood, fluid and electrolyte levels, and immobilization.

The ages of the 67 patients who were followed ranged from 18 days to 24 years, the average being 11 years; 96 per cent were less than 21 years old. Forty-eight (72 per cent) were males and 19 (28 per cent) were females.

The infecting organism was determined, either by culture of the blood or aspirated material, in 58 cases (86 per cent). Hemolytic *Staphylococcus*

FIG. 5

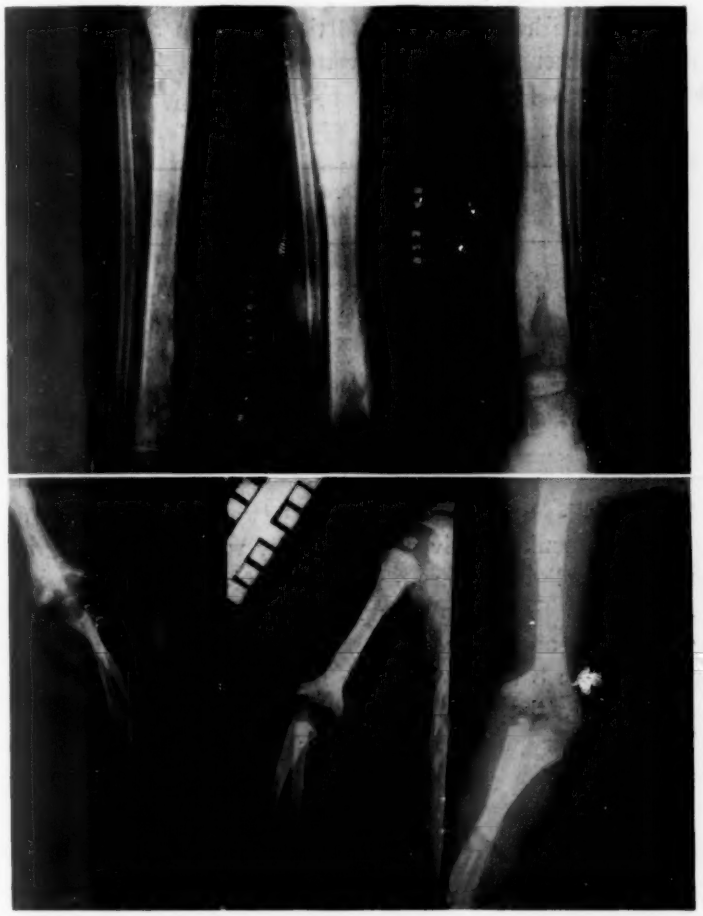

FIG. 6

FIG. 5.—Fair result obtained in C. W., white boy, age 14 years. Serial roentgenograms, showing persistent osteoporosis coupled with sclerosis and eburnation, taken February 6, 1948, September 23, 1948 and June 2, 1949.

FIG. 6.—Fair result obtained in J. M., Negro girl, 18 days old. Roentgenograms taken August 12, 1946, November 15, 1946 and May 7, 1948. Note residual deformity resulting in cubitus valgus and subluxation of radius.

aureus was cultured in 48 cases (83 per cent) and nonhemolytic *Staphylococcus aureus* in four cases (7 per cent). Hemolytic Streptococcus was recovered in two (3 per cent) and nonhemolytic Streptococcus in three (4 per cent) cases. A pneumococcus of undetermined type was isolated in one case and an unidentified coccus in another.

The femur was involved in 28 cases, the tibia in 24, the humerus in nine, the fibula in five, the radius in three, the ulna in two, the patella in two, and the os calcis and ilium in one each, making a total of 75 bony lesions in the 67 cases. Multiple bones were involved in seven cases (10 per cent) and pyoarthrosis complicated nine cases, the hip being involved in four of these, the knee in four and the elbow in one. Septic pulmonary and renal infarcts were present in seven cases. Positive blood cultures were obtained in 21 cases (31 per cent).

TABLE I.—*Results of Closed Method of Treatment of 75 Bony Lesions in 67 Patients with Acute Hematogenous Osteomyelitis.*

Result	Cases	%	Treated		
			Within 5 Days	5–10 Days	10 Days
Excellent	28	37.3	21	7	0
Good	34	45.3	18	16	0
Fair	8	10.6	2	5	1
Poor	5	6.7	0	3	2
Total	75		41	31	3

The amount of penicillin given systemically varied from 920,000 to 8,640,000 units. The smallest amount of penicillin given locally was 200,000 and the largest amount 6,600,000 units. Two patients received no penicillin locally because no abscess could be located. The duration of penicillin therapy ranged from 8 to 48 days, the average being 24 days.

As suggested by the report of Altemeier and Wadsworth,[3] the results were evaluated in terms of damage to the bones involved and were classified as excellent, good, fair or poor. Results were considered *excellent* if roentgenograms showed restoration of normal architecture of bone or minimal thickening of trabeculae, no osteoporosis, no recurrence, and normal function. Results were classified as *good* if roentgenograms revealed moderate sclerosis, no persistent sequestra or cloaca, no recurrence and no dysfunction. Results were rated as *fair* if roentgenograms revealed sclerosis or persistent osteoporosis and cloaca with some persistent deformity of the bone. If the size or persistence of the abscess cavity required surgical drainage or later sequestrectomy, or if there was a recurrence of the bony infection, the result was classified as *poor*.

Table I gives the results of treatment of the 75 bony lesions in the 67 patients. It will be noted that in 62 of the 75 lesions (82 per cent) the result

was excellent or good. In eight (10 per cent) the result was only fair and in five (6 per cent) it was poor. It is significant that the greatest number of excellent and good results occurred in those patients who received penicillin within five days of the onset of illness. Conversely, the five failures occurred in those in whom penicillin therapy was not begun until after this five day period.

DISCUSSION

Infections that presented difficulties in treatment fell into several well defined groups, which will bear brief discussion. The highest percentage of good and fair results was obtained in the group in which adequate penicillin therapy was begun during the first five days of illness. It can thus be concluded that the earlier a presumptive diagnosis of osteomyelitis can be made and sufficient penicillin given, the less damage to bone will occur. Undoubtedly, some patients with hematogenous infection from the *Staphylococcus aureus* who have pain and tenderness in the bone but receive penicillin within the first 24 to 48 hours never show demonstrable osseous changes. Hence, it is extremely important to give penicillin upon the slightest suspicion of acute osteomyelitis.

Small amounts of penicillin (less than 30,000 units every three hours) given during the first few days serve only to ameliorate symptoms without preventing localization of the bacteria in bone with slow development of bony necrosis and abscesses. If the early symptoms and signs in a given case are sufficient to justify a presumptive diagnosis of osteomyelitis, adequate doses of penicillin should be given from the outset. Discontinuation of the drug too soon may result in recurrence or persistence of the local infection.

In six of the entire series of 94 patients, or about 6 per cent, the organisms recovered from the blood or aspirated material proved to be penicillin-resistant. In such cases other antibiotics must be substituted if good results are to be obtained. Therefore, every effort should be made to identify the infecting organism at the beginning of treatment and test its susceptibility to penicillin.

Failure to locate secondary foci in bones or joints other than the one first found sometimes prolongs the course of the disease and leads to extensive damage to bone. Patients usually respond promptly if secondary foci are found, pus is aspirated and penicillin is instilled into the joint or abscess cavity.

Since sequestra revascularize in many patients treated with penicillin, it is desirable to follow the course of the disease by serial roentgenograms rather than to institute surgical measures as soon as the sequestra first appear. Their removal is indicated by persistent clinical signs of localized infection over the site of the sequestra together with roentgenographic evidence of complete and persistent separation.

If a focus is recognized in the neck of the femur, especially in those cases in which penicillin therapy is begun after five to ten days, the hip should be

protected by traction for several weeks because, if the neck of the femur is softened by necrosis, the head is soon separated by the muscular spasm and then becomes a free sequestrum in the hip joint. Such a complication usually requires removal of the dead head with subsequent serious impairment of the hip.

SUMMARY

Sixty-seven patients with acute hematogenous osteomyelitis, in whom there were 75 bony lesions, have been treated with penicillin systemically and locally without surgical drainage.

Roentgenograms made on an average of 21 months after treatment showed little or no residual changes in 60 of the 75 bony lesions (80 per cent). Poor results, as indicated by sequestra which required later removal, or by recurrent infections, occurred in five bones (7 per cent).

In view of the excellent results obtained by the closed method of treatment it would appear unnecessary to drain localized abscesses surgically with the possible exception of a few extensive abscesses or those associated with detached sequestra.

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DISCUSSION.—DR. EDWIN P. LEHMAN, Charlottesville, Va.: Doctor Caldwell should be congratulated on his results. I like to think of osteomyelitis as divided into two phases, one of which the surgeon rarely sees. Those are the cases which are seen within the first 24 or 48 hours of the infection, before there is any obvious change in the soft tissues overlying the bone. The clinical picture is one of general sepsis and localized tenderness. The pathologic condition is one of unlocalized marrow infection, a cellulitis of the marrow. A general principle in the surgical treatment of infections is that there should be decompression of infections in closed spaces where pressure itself is inimical to localization by limiting blood supply. Of course the bone marrow is a closed space where this fundamental principle is of primary importance. If one can decompress the

bone marrow in the early stages of infection one can often prevent necrosis of hard bone. The occurrence of chronic osteomyelitis may be aborted.

We feel that in those cases seen within a short time after onset, before there has been time for much change in the circulation of the hard bone, decompression—not drainage or exploration—is a desirable procedure, supplemented, of course, by penicillin. In such cases one will see a prompt disappearance of sepsis, and a prompt disappearance of pain, in spite of a fresh soft tissue wound, and a positive culture from the undisturbed bone marrow, usually *Staphylococcus aureus hemolyticus,* with prompt and uncomplicated recovery and absolutely no later change in the bone itself except for the healing window. It is a limited group as the surgeon sees it, but I would like to point out the advantages of surgical procedure in that group of cases.

Dr. Charles S. Venable, San Antonio, Texas: I am usually a very agreeable sort of fellow, but at the moment I am afraid I am not going to be able to agree entirely with my friend Doctor Caldwell. In the first place I do not believe that with surgery, antibiosis, or any other method, osteomyelitis is ever cured. It may only be arrested in various stages. He has shown some skiagrams of progressive arrest. In the terminal of each of his skiagrams you have been able to see areas that are only under arrest. Those areas some day, some time, with trauma, infection by a cold, stubbing a toe, or for no known reason, may become hot and red and feverish and break down and start all over again.

Antibiosis is supposed to cover all sins of men, women and children, but it doesn't. Penicillin is the antibiotic that is prescribed for babies when the mothers phone to the pediatrician; and from there, all the way on, everybody gets penicillin. I have had for several years the opportunity of working at Brooke General Hospital, in which there is a septic center that is under very close supervision and controlled work in research, and we find that penicillin and sulfathiazole, either independently or combined, are a very small fraction of the antibiotics or combinations of antibiotics that will arrest many of these bone infections. In this service there are some 80 beds that run an average of 60 beds full; they are all septic wounds. I would say there are not more than 15 to 20 per cent that come under the head of general surgery as we understand it, and I should not go beyond that phase because I am not an orthopod, I am just a country doctor and a general surgeon. We find that a large percentage of osteomyelitis cases have broken down, after having been previously arrested. We do not see many acute cases.

I know that Doctor Caldwell's paper concerns children, but I think osteomyelitis is a much broader subject than just children. I think it is wrong to anticipate that we can arrest this in children, because these children are going to be the old men in the Veterans Administration and all down the line, with a breakdown of their disease unless they are really cured. We know we can do better than just arrest the condition, with antibiosis properly controlled and properly watched with blood cultures daily, and we will find there is a change in the type of antibiotics used; we may use streptomycin, aureomycin, chloromycetin, bacitracin, sulfonamides, penicillin or various combinations. Unless the case is followed day by day and week by week, with cultures, it is impossible to know what is being accomplished and what antibiosis is needed. When the wound is brought under control, then it may be filled with bone chips step by step and closed, so that in six or eight or ten weeks it is healed, and you cannot see by roentgen ray where the lesion was. These cases will not be repeaters. But I think to leave them as potential breakdowns is wrong teaching.

Dr. Mims Gage, New Orleans: I certainly agree with Doctor Caldwell's principles of management of traumatic or secondary osteomyelitis. Of course, there is a great difference between the pathology and mode of extension of primary hematogenous osteomyelitis and traumatic or secondary osteomyelitis. The primary or hematogenous type involves the metaphasis, whereas the traumatic type involves the traumatized

osseous tissue which in the majority of cases involves the shaft. I do not believe that there is ever the destructiveness in the traumatic type as in the primary form.

I consider immobilization, chemotherapy and antibiotics, with supportive therapy, *i.e.*, blood transfusions, fluids and electrolytes, as advocated by Doctor Caldwell, the management of choice in these cases. The same type of treatment should be used for the primary forms—surgical measures being indicated only when drainage becomes necessary. The sequestrum, when formed, if producing symptoms, can be removed in the quiescent stage.

In both the traumatic and primary types of osteomyelitis, early use of the bacteriostatics, (sulfonamides and antibiotics) will inhibit bacterial growth, but will not neutralize the necrogenic bacterial toxins that are the actual cause of bony destruction. I believe we shall always have bony destruction in both types, even though bacterial growth is inhibited. The reason for this is that we do not have a potent antitoxin, which is so necessary as an adjunct to chemotherapy and antibiotic therapy in osteomyelitis. Before the sulfonamides or antibiotic bacteriostatics became available, I treated the primary form by immobilization, transfusions and autostaphylococcal serum with excellent results (Acute Hematogenous Osteomyelitis, Surg., Gynec. & Obst., **75**: 123, 1943). I think that a potent autostaphylococcal serum has a reservel place in the treatment of certain cases of osteomyelitis.

The methods of treating traumatic osteomyelitis in the past war have been of inestimable value in civilian practice. These principles have been utilized by Doctor Caldwell and his associates with the excellent results that he has just reported. I wish to congratulate him for his excellent presentation. I will have to stop using an old phrase that I have used for years and that is "The commonest etiologic factor and most constant propagator of chronic osteomyelitis is the surgeon."

Dr. Jack Wickstrom, New Orleans (closing): I wish to thank Doctors Lehman, Venable and Gage for their consideration and criticisms of this paper, on behalf of Doctor Caldwell and myself. I believe that in the plan of treatment we have used, we have relied upon circulating antibiotics during the first 24 to 48 hours to control propagation of bacteria and production of toxin, and have solved the problem quite well without decompression. We feel that once the circulation in the bone locally has been altered by thrombosis of the adjacent vessels or by pressure within a forming abscess cavity, decompression by aspiration of a subperiosteal lesion or a subcortical lesion in cancellous bone is effective and desirable.

We have no disagreement with Doctor Venable concerning change of antibiotics when indicated by altered bacterial sensitivity. However, we cannot possibly agree with his contention that the residual sclerosis which was shown in some of these roentgen rays is an indication for surgical excision of this scarred bone and replacement with cancellous chips. The vast majority of these patients are well, have no residual dysfunction or evidence of infection. It would be impossible for us to convince them or ourselves that surgery, as described by Doctor Venable, was indicated or would be beneficial. We have had a little experience with streptomycin, more experience with aureomycin. These cases have not been followed long enough to draw definite conclusions.

Doctor Gage might be interested to know that in two of these patients the infection seemed to be controlled by penicillin; the organism which was isolated was penicillin sensitive and yet these patients remained extremely toxic. We used Staphylococcus antitoxin that he mentioned on these two cases, with very gratifying results and improvement of the patient's general condition.

The introduction of new antibiotics is so rapid that I doubt if all of us can keep up with them. We certainly have been unable to evaluate them accurately; however, they are proving to be exceptionally valuable adjuncts in the control—if not the principal means of treatment—of infection in bone if it is seen early.

LACERATION OF PAROTID DUCT; FURTHER EXPERIENCES*

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PRIOR TO 1949 nine instances of successful primary repair of a severed parotid duct had been reported in detail.[1-8] In the eight reports covering these nine cases many technical variations were described. Emphasis was generally placed upon the importance of an intraluminal dowel traversing the line of anastomosis. Postoperative sialography was performed in only one case of the nine.

In May, 1949, three instances of successful primary repair were reported.[9] Each anastomosis was performed over a ureteral catheter which was removed immediately through the ostium; anastomoses were accomplished with sutures of six-zero eye silk on a small cutting needle. Wounds were closed without drainage. Patients were allowed food promptly; adjunctive measures consisted of penicillin and mouthwashes. In each of these three cases primary healing occurred; proof of successful repair was established by postoperative sialography and by demonstration of salivary flow from the ostium of the duct.

The technic differed in principle from those previously described in only three particulars, viz., the early withdrawal of the catheter, the use of finer suture material, and the early institution of a feeding regimen designed to stimulate rather than to suppress the flow of saliva.

The present report deals with nine additional cases in which repair of a severed parotid duct has been undertaken. In final analysis of results these nine cases are considered collectively with the three previously reported.

Injury to the parotid duct should be suspected whenever lacerations of the face cross a line which extends from the inferior border of the external acoustic meatus to a point midway between the ala of the nose and the upper border of the lip. This line is a satisfactory guide to the position of the duct except that the proximal end of the duct usually occupies a somewhat lower position as it emerges from the gland, and then curves upward and forward for a short distance. Sometimes it is possible at the initial inspection of the wound to see the cut ends of the duct. Salivary flow is often apparent from the proximal cut end; this may appear spontaneously, or may be elicited by pressure over the gland. In cases of injury to the duct where the diagnosis is uncertain it is usually possible to thread a ureteral catheter into the ostium and up the duct until the tip appears in the wound. This has been accomplished in the receiving room in five of 12 cases. Although the ostium is ordinarily visualized with ease, it may be obscured by mucosal folds; occa-

* Read before the Southern Surgical Association, Hot Springs, Virginia, December 6, 1949.

sionally one may catheterize the ostium readily, only to find that the catheter cannot be made to traverse the lax and tortuous portion of the duct which extends from the ostium through the buccinator to and around the anterior border of the masseter muscle. This same obstacle may be encountered in attempts at retrograde passage of a catheter introduced in the distal cut end of the duct.

Injuries in the masseteric portion of the duct are the most frequent, and are the most favorable for repair. In this part of its course the duct is straight and relatively immobile, and its walls are thick and tough. As a rule the masseter muscle is cut also; it can be repaired with ease, since it presents a dense tendinous surface in this region. In the vicinity of the parotid gland the wall of the duct becomes much thinner and anastomosis becomes more difficult; moreover, this portion of the duct may be obscured by the overhanging anterior margin of the gland.

Attempts at primary repair should be regarded as successful only if subsequent salivary flow is demonstrated and the duct system shown to be patent by sialography. According to these criteria, primary repair has been accomplished in eight of 12 patients, of whom three have been reported previously. Successful repair is presumptive in the ninth case, a child now four years of age, in whom sialography has not been feasible because of the diminutive size of the ostium.

There follows a summary of each of the cases in which successful repair has been accomplished, exclusive of the three cases previously reported. In general, the technic of repair has not differed significantly from that previously reported. In three cases of this group, however, a catheter could not be passed through the distal segment of the divided duct. This difficulty has been overcome by the use of a silver wire probe* in place of a catheter. On each occasion the wire probe has been passed readily, the anastomosis then being performed over the wire.

CASE REPORTS (GROUP I)—SUCCESSFUL PRIMARY REPAIR WITH UNCOMPLICATED HEALING

Case 6.—C. M., male, Negro, age 19, in whom extensive multiple lacerations of the left face were incurred March 6, 1949, as a result of injury with broken glass. A No. 3 ureteral catheter was introduced in the ostium of the left parotid duct; the tip of the catheter appeared in one of the facial wounds. The laceration of the duct was situated just anterior to the parotid gland. Facial movements were normal. The duct was repaired over the catheter with interrupted sutures of six-zero eye silk. The catheter was removed at the conclusion of the anastomosis. There was no injury to the parotid gland. The wound was closed in layers with interrupted sutures of number 100 cotton. A sialogram on the fifth day showed good filling of the duct system; the site of the anastomosis could not be detected (Fig. 1).

* Graduated sizes of flexible silver wire of the type ordinarily employed as sutures have been cut into lengths of approximately one foot each, and their ends smoothed with crocus cloth, thereby creating double-ended probes of varying diameters. Sizes 16 to 20 will provide an adequate range (diameters 0.05" to 0.03").

Case 7.—D. B., female, white, age 3, suffered laceration of the right face from the angle of the mouth to the region of the ear on April 13, 1949, from broken windshield glass. The parotid duct was severed in its mid-masseteric portion. The upper portion of the parotid gland was cut. There was right facial paralysis. An attempt to thread a No. 3 ureteral catheter through the cut distal end of the duct was unsuccessful. A segment of No. 20 silver wire (diameter 0.032″) was passed with ease; anastomosis of the duct was performed over the wire, which was then withdrawn. The facial wound was closed in layers. Healing was uncomplicated. There has been no swelling in the parotid region at any time. One attempt at postoperative sialography was abandoned because of inability to catheterize the tiny ostium. Facial movement was almost completely restored within 3 months. The patient remains well 7 months after injury. Successful repair is presumptive. This is thought to be the first report of repair of a parotid duct in a child.

Case 8.—R. R., male, white, age 40, had a long vertical knife wound inflicted just anterior to the left ear on April 17, 1949. There was paralysis of the left face. There was extensive laceration of the substance of the parotid gland. The major parotid duct could be identified within the cut surface of the gland. In this area the wall of the duct was quite thin in contradistinction to the thick tough walls regularly encountered in the masseteric portion. A soft silver wire, size No. 18 (diameter 0.04″) was passed into the distal cut end of the duct and was carried through the ostium without difficulty. The other end of the wire was threaded into the proximal cut end of the duct. Anastomosis of the duct was accomplished over the wire, which was then removed. The capsule of the gland was closed tightly with closely spaced sutures of No. 100 cotton. Fascia and skin were closed without drainage. Healing was uncomplicated. Copious salivary flow from the ostium was demonstrated during the postoperative period. At the end of 3 months salivary flow was still readily demonstrated. Sialogram at this time showed moderate stricture at the anastomotic site, with some proximal dilatation of the duct system (Fig. 2). Pronounced recovery of facial movement was apparent.

Case 9.—F. S., male, Negro, age 23, sustained a vertical knife wound in the upper portion of the left cheek on August 6, 1949. A No. 3 ureteral catheter was introduced in the ostium of the duct; the catheter tip appeared in the wound. Anastomosis of the mid-masseteric portion of the duct was accomplished over the catheter. A laceration of the anterior surface of the parotid gland was closed. The wound was closed without drainage. There was no facial weakness. Recovery was uncomplicated. Salivary flow reappeared promptly. A sialogram on the eighth day showed good filling of the duct system (Fig. 3). Three month follow-up has been without incident.

Case 10.—I. T., female, Negro, age 28, received a vertical laceration in the mid-portion of the left cheek (knife or razor) on September 10, 1949. A No. 3 ureteral catheter introduced through the ostium of the left parotid duct appeared in the wound. The duct was severed just proximal to its passage around the anterior border of the masseter muscle. There was no facial paralysis, and the parotid gland was uninjured. Salivary flow was demonstrated on the third day after anastomosis. A normal sialogram was obtained on the eighth day (Fig. 4). Recovery has been without incident.

Case 12.—M. de la T., male, Latin-American, age 16, suffered knife or razor wound on October 9, 1949. The wound involved the left face from the tragus to the lower lip. A No. 3 ureteral catheter was introduced in the ostium of the parotid duct but could not be made to bend around the masseter muscle. The proximal end of the severed parotid duct projected conspicuously in the wound, into which it could be seen to discharge saliva. The parotid gland was extensively incised. There was no facial paralysis. An attempt at retrograde passage of a No. 3 ureteral catheter was unsuccess-

FIG. 1

FIG. 2

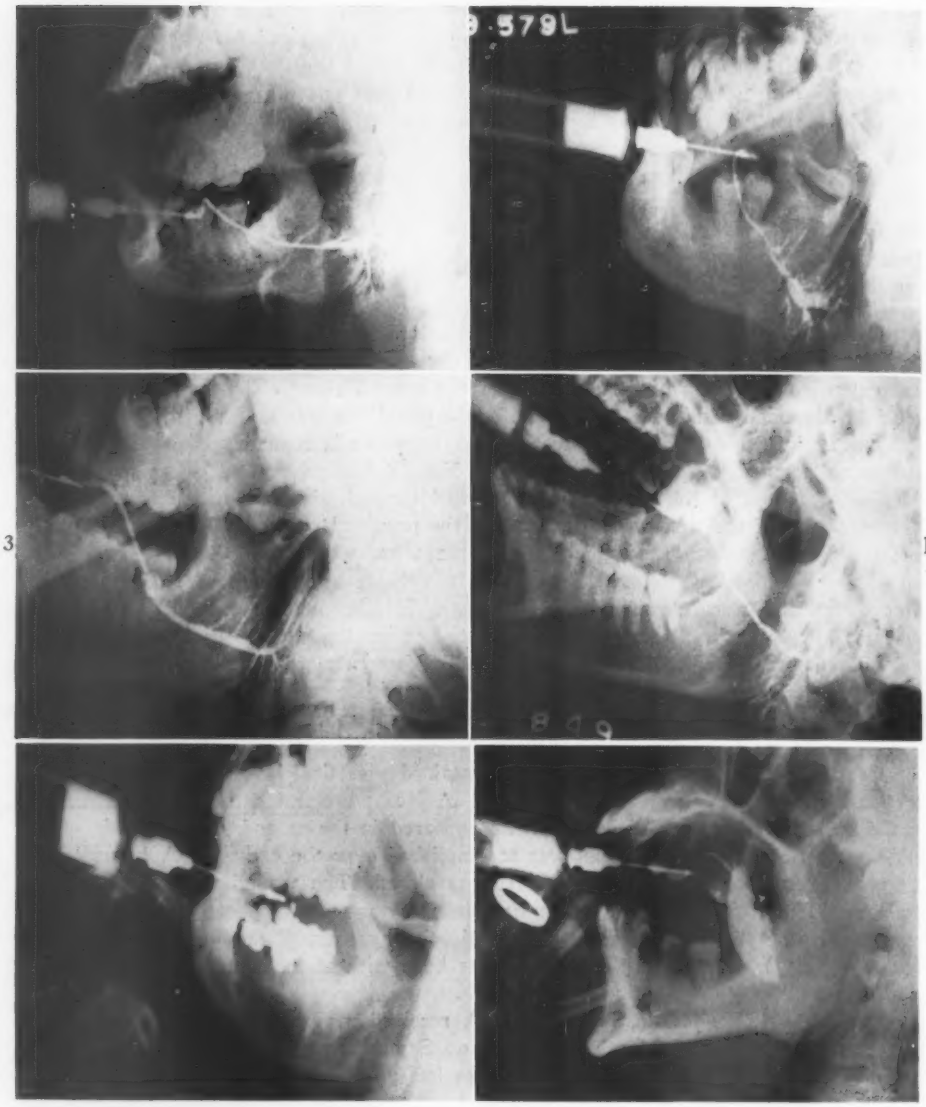

FIG. 3

FIG. 4

FIG. 5

FIG. 6

FIG. 1. (Case 6)—Sialogram five days after repair of parotid duct.

FIG. 2. (Case 8)—Sialogram three months after repair of major parotid duct within substance of gland. Constriction is apparent at anastomotic site, with some proximal dilatation.

FIG. 3. (Case 9)—Sialogram eight days after repair of parotid duct.

FIG. 4. (Case 10)—Sialogram eight days after repair of parotid duct.

FIG. 5. (Case 4)—Subcutaneous salivary fistula eight days after unsuccessful primary repair of parotid duct.

FIG. 6. (C. E.)—Subcutaneous salivary fistula four days after laceration of parotid duct. Injury to duct was not recognized at time of initial repair of facial wound.

ful. A segment of silver wire was passed with ease, and repair accomplished over the catheter at the mid-masseteric level. The capsule of the parotid gland and the layers of the face were closed with closely spaced fine silk sutures. A sialogram on the seventh day was normal, and healing was uncomplicated.

Local infiltration anesthesia has been entirely adequate in all the foregoing operations, exclusive of that performed upon the child, wherein a general anesthetic was employed.

It is immaterial whether the catheter be passed via the ostium into the wound or in a retrograde direction from the cut end of the duct into the mouth. In this series, whenever the catheter was passed via the ostium as a preliminary diagnostic measure, it was allowed to remain in place for use in the subsequent anastomosis; where the diagnosis was obvious, catheterization was deferred until the time of repair, at which time the catheter or wire was passed retrograde from wound to mouth. The latter method may be a less likely source of contamination.

Sutures of six-zero eye silk on atraumatic curved cutting needles have been used for all anastomoses. The consistency of the duct wall is too dense to permit easy passage of any needle other than a cutting one. In the former report it was recommended that the sutures not be allowed to penetrate the lumen of the duct; this is no longer regarded as feasible or necessary. Interrupted sutures are preferred to mattress sutures, since constriction is a more likely complication than leakage.

In three cases the attempt at primary repair and restoration of function failed. In one of these (Case 5) failure was functional only, since the wound underwent primary healing; subsequent sialography showed the duct to be occluded. In each of the other two cases (Case 4 and Case 11) the formation of a subcutaneous collection of saliva was quickly apparent following attempted repair. The manner in which these complications were dealt with is outlined below.

CASE REPORTS (GROUP II)—ATTEMPTED PRIMARY REPAIR WITH FAILURE

Case 4.—O. A., male, white, age 35, suffered laceration of the left face January 30, 1940, from windshield glass. The wound extended from the upper lip to the tragus. An unsuccessful attempt was made to catheterize the parotid duct via the ostium. There was paralysis of the left face. The duct was severed in the zone of its curvature around the anterior border of the masseter muscle; in this area the angulation of the duct is pronounced. A No. 4 ureteral catheter was passed retrograde into the mouth. Anastomosis was performed over the catheter in the usual fashion. A small laceration in the substance of the parotid gland was repaired, and the wound was closed without drainage. Within 48 hours it was apparent that there was a collection of fluid in the subcutaneous tissue. On the fifth day the subcutaneous salivary tumor was aspirated, with recovery of 5 cc. of clear yellow fluid. Aspiration was repeated on the sixth, seventh, and eighth days, during which time no discharge of saliva could be observed from the ostium. A sialogram on the eighth day showed no demonstrable filling of the duct, and the oil formed a subcutaneous pool in the area of the salivary tumor (Fig. 5). Daily aspiration was continued until the eleventh day. The wound was covered at all times with a collodion seal in an attempt to prevent the formation of an external fistula. Secondary

operation was performed 11 days after injury. The anastomosis was intact in all areas except in the outer aspect of the curvature of the duct. At this point approximately one-fourth of the circumference of the duct was open and draining. The repair was taken down and a new anastomosis was performed, using small mattress sutures. By the third day some salivary secretion was observed from the ostium. On the fourth day, however, it was apparent that there was again a subcutaneous salivary collection. Sialogram on this day showed pooling of the oil in the subcutaneous tissue, but in addition there was filling of the duct system. Moreover, salivary secretion from the ostium was demonstrated with ease. Since it had been demonstrated that saliva was flowing both into the the mouth and into the subcutaneous tissue, it was felt that if the formation of an external fistula could be avoided or discouraged, the sole passageway into the mouth might be re-established. Accordingly, a collodion seal was maintained over the skin incision. There was occasional slight external leak of saliva, but by the twelfth day external drainage had ceased, and did not subsequently recur. There was no swelling of the parotid region at any time. The patient was seen at 6 months and at 9 months. At each of these examinations the ostium was dry. Catheters and cannulas could be introduced for a distance of one centimeter, but would not go beyond this point, and no oil could be introduced. It was concluded that the duct was closed at the site of injury. Recovery from facial paralysis was relatively complete and the patient was free of any discomfort.

Case 5.—O. B., female, Negro, age 24, received multiple lacerations of the left face in an automobile collision on February 13, 1949. The parotid duct was severed just distal to the anterior margin of the parotid gland, where its walls were thin. There was an associated laceration of the gland. There was no facial paralysis. A No. 4 ureteral catheter introduced in the distal cut end of the duct could not be made to traverse the portion of the duct between the anterior border of the masseter muscle and the ostium (this was the first case in which passage of a catheter was unsuccessful; in subsequent cases this difficulty was overcome by the use of segments of soft silver wire as previously described). A long strand of stainless steel wire was doubled, and the angulated end passed into the duct. It traversed the length of the duct with ease, and appeared in the mouth. The two free ends were placed in apposition and tucked in the butt end of a No. 4 ureteral catheter. By simultaneous traction on the wire and pulsion on the catheter, it was possible to pass the catheter through the distal segment of the divided duct. Anastomosis was accomplished over the catheter in the usual way. The laceration in the gland was closed with closely spaced interrupted cotton sutures, and the wound edges were approximated without drainage. On several occasions following the operation salivary flow was demonstrated from the ostium. The wound healed uneventfully. Two weeks after repair a cystic swelling 2 cc. in diameter appeared in the region of the parotid gland. After 3 months the cyst began to diminish in size and by 6 months it had disappeared entirely. The patient remains clinically well after 9 months. A cannula may be introduced in the ostuim with ease, but no oil can be injected and no salivary secretion is observed. It is assumed that the duct has become completely occluded. This case represents a failure of restoration of function. However, from the clinical standpoint healing has been uncomplicated and the result is satisfactory.

The development of obstruction of the duct in cases 4 and 5 was interesting and unexpected. It had been feared that such a complication would lead to cyst formation. However, since no swelling of the parotid region has occurred it is to be presumed that the gland has undergone atrophy in each instance. This occurrence immediately suggests the possibility of purposeful obstruction of the duct by ligation as a simple means of dealing with fistulas

of the duct, or with recent injuries where conditions do not favor primary repair.

There is ample precedent for the procedure of ligation of the duct as a means of definitive therapy. In 1917 Morestin[10] described his experiences with 62 cases of salivary fistula secondary to war wounds; 30 involved the gland and 32 arose from the duct. Numerous instances were described by this author in which fistulas of either the gland or duct underwent spontaneous cure as a result of cicatricial obstruction. Glandular fistulas were generally much easier to deal with than those of the duct. Morestin expressed his belief that in many patients subjected to reconstructive procedure the good result obtained was due to obstruction of the duct with physiologic death of the gland rather than to success in permanently re-routing the salivary drainage. Accordingly, he eventually adopted surgical ligation of the duct as the procedure of choice in persistent fistulas of the duct despite his extensive antecedent experience in creation of internal fistulas. This operation was performed on 13 cases; in 11 prompt healing occurred; in two there was transient collection of saliva, with disappearance after aspiration or drainage. He was eventually led to the following conclusions regarding the management of salivary fistulas: for persistent fistulas of the gland, excision of the fistula and of all surrounding cicatricial tissue should be done with tight closure of the margins of the gland; for persistent fistulas of the duct, excision of fistula and surrounding scar, ligation of the duct, and closure without drainage should be performed. He stressed the importance of deferring operative treatment to allow the fistula an opportunity to undergo spontaneous closure. He conceded that injuries of the anterior part of the duct might be treated equally well by creation of an internal fistula, but expressed doubt that such fistulas would remain functional.

Ivy,[11] in 1918, commented upon the frequency with which glandular atrophy and arrest of parotid secretory function followed spontaneous occlusion of the duct by cicatrix. He mentioned ligation of the duct as a measure to be employed in the treatment of fistulas of the duct when internal drainage could not be brought about.

It is generally conceded that infection of the duct system tends to perpetuate the fistulous discharge of saliva. It is probable that greater emphasis should be placed upon the maintenance of an intact skin envelope as a means of preventing infection when an external fistula is impending. A case report is interpolated at this point to illustrate this principle and to show the tendency of the duct to undergo spontaneous occlusion. Since there was no attempt at repair of the severed parotid duct, this patient is not numbered in the present series.

Case Report.—C. E., male, white, age 39, was first seen on July 5, 1949, 3 days after injury of the left face with broken glass. At the time of injury the cutaneous wound had been sutured without drainage. At the time of the patient's initial visit it was apparent that there was a collection of fluid in the subcutaneous tissue of the cheek. On the fourth day after injury saliva was aspirated from the cheek, and a sialogram

was performed which showed diffusion of oil from a laceration which appeared to be in the posterior portion of the duct (Fig. 6). The program thereafter consisted of application of collodion gauze to the external wound and aspiration of the salivary tumor at intervals of 3 days. The establishment of an external fistula was averted except for occasional loss of a small amount of fluid from the needle puncture wounds. The last aspiration was performed on the fourteenth day. There have been no residual symptoms other than facial paralysis, which is improving. At three months an attempt was made to repeat the sialogram; the ostium was cannulated without difficulty, but no oil could be introduced. The duct was considered to be occluded; the parotid gland was not palpable.

It is possible that the work of Morestin has been lost sight of, since descriptions of new reconstructive procedures for the management of parotid fistulas continue to appear in the literature with relative frequency. The limited experience of the author in the foregoing three cases has been consistent with that of Morestin.

The final case of failure of primary repair presents the additional problem of failure of the subcutaneous fistula to subside on conservative treatment.

Case 11.—L. T., male, Negro, age 49, suffered laceration of the right face with a knife on September 28, 1949. There was a short transverse laceration beginning in the ear lobe and extending forward. There was paralysis of the right face. A No. 5 ureteral catheter was passed into the ostium of the parotid duct; the catheter tip appeared in the wound. The duct injury was located just beyond the emergence of the duct from the gland, and was overhung by the projecting anterior margin of the gland, which was also cut. The duct was cut at a very long bevel, making anastomosis difficult. The parotid gland was repaired and the wound was closed without drainage. Gradual swelling of the cheek ensued. A collodion dressing was maintained over the skin wound at all times. Repeated examinations of the ostium failed to disclose salivary secretion at any time. Aspiration of the cheek was performed on the ninth day with recovery of 15 cc. of clear yellow liquid. Sialogram on the tenth day showed good filling of the distal portion of the duct with pooling of the dye at the site of the laceration. Aspiration of the subcutaneous fistula was continued at intervals of 3 days, with recovery of 15 to 20 cc. of yellow liquid on each occasion. At the end of 7 weeks the rate of accumulation of fluid was unchanged. There had been no external drainage of saliva at any time, and the skin wound was healed. Decision was made to attempt ligation of the duct proximal to the site of the fistula. The wound was reopened under local anesthesia. Identification of structures was very difficult. The fluid was contained in a cyst-like space having a distinct outer wall and a moist, glistening lining; it was not possible to determine whether it was intra- or extra-glandular. In its base there could be seen the sutures of the previous anastomosis, but the duct proper could not be identified. No single point of secretion could be detected. The surface and margins of the wall were excised, leaving the base. Several fine cotton sutures were placed in what appeared to be the region of the duct, in the hope that obstruction of the proximal end of the duct would be achieved. The wound was closed in layers and sealed with collodion. Subsequent to operation the salivary tumor did not reappear. On the seventh postoperative day aspiration was performed with recovery of 4 cc. of bloody fluid; this was repeated on the twelfth day with the same result. Healing thereafter was without incident. It is not known whether actual ligation of the duct was accomplished, or whether occlusion has resulted from cicatrix. The difficulty of re-operation in such a distorted field deserves emphasis. If a similar beveled laceration in the thin portion of the duct were encountered at this time, it would probably be treated by ligation at the initial operation rather than by attempted primary anastomosis.

DISCUSSION

Successful primary repair of a severed parotid duct with restoration of function can be accomplished without undue difficulty in a relatively large proportion of clean incised wounds. If laceration of the duct is suspected, its existence can be verified by simple measures. It is recognized that many undiagnosed and untreated lacerations of the gland or of the duct may proceed to uneventful healing, and that established fistulas may also disappear spontaneously following occlusion of the major or tributary ducts by cicatrix. There remain, however, many persistent fistulas which are refractory to healing and difficult of correction. The occasional prevention of such fistulas is adequate justification for the effort involved in early recognition and attempted repair of injuries of the parotid gland or duct.

Injuries of the duct are frequently complicated by associated injuries of the gland substance, and by damage to the facial nerve. In the current series of 12 cases of duct injury, there were eight associated injuries of the parotid gland and seven instances of seventh nerve injury sufficient to produce pronounced degrees of facial paralysis.

It is possible that successful repair of a parotid duct might be complicated by the development of a fistula from an associated laceration of the gland. The fact that there has been no apparent glandular fistula in this series is attributed to tight closure of the parotid capsule and the avoidance of infection. The injuries, being sharp incised wounds, were generally favorable to primary healing.

No attempt at facial nerve reconstruction has been made in any case, since no nerve fibers could be found having sufficient size to permit either their anastomosis or the employment of a directional suture. Nevertheless, in six cases spontaneous restoration of facial movement has occurred to a relatively complete degree. The seventh patient is now in his second month since injury, and as yet has shown no recovery.

The primary management of clean incised wounds which involve the parotid duct may be outlined as follows:

1. Primary repair of the duct over a catheter or wire, using interrupted sutures of number six-zero silk.
2. Tight closure of lacerations of the parotid gland.
3. Careful layer approximation of the facial laceration without drainage.
4. Prompt removal of the catheter or wire.
5. Adjunctive measures designed to stimulate secretory activity of the gland and to inhibit infection (food, penicillin, mouthwashes, etc.).
6. In instances where the ends of the duct are destroyed, ragged, beveled, or otherwise unfavorable to primary repair, ligation may be performed with safety.

In instances where primary repair has failed, or where parotid duct injury has been unrecognized at the time of repair of a facial laceration, the following outline of management is suggested:

1. Attempt to avoid the development of an external fistula by repeated aspiration of the salivary collection and by the constant application of collodion gauze to the margins of the skin wound.

2. Continue the above management for a period of several weeks in the hope that spontaneous occlusion of the duct will occur.

3. In instances where the foregoing plan is not successful, re-operation with proximal ligation of the parotid duct is a satisfactory method of correcting a persistent fistula.

The author has made no attempt thus far to evaluate roentgen ray therapy as a means of definitive treatment of fistulas of the parotid duct. It is possible that roentgen ray might be as effective as surgical ligation, or that it might be a useful form of adjunctive therapy. Nor has it been possible in this series of cases to assess the relative merits of ligation as opposed to the creation of an internal fistula in the management of established parotid fistulas. This has already been dealt with extensively by Morestin. The limited experience gained in this series confirms Morestin's findings to this extent—that occlusion of the major duct may come about spontaneously and that there is apparently no adverse effect from such an occurrence. In view of the variety of complicated procedures which are still advocated for the correction of parotid fistula it is possible that the observations made by Morestin have been obscured to some degree by the elapse of 32 years, and that the extensive series of cases reported by him should be reviewed by those interested in this field. The more complicated surgical procedures may possess the additional disadvantage of subjecting the filaments of the facial nerve to further damage in a distorted field where their recognition is difficult.

SUMMARY AND CONCLUSIONS

Primary repair of a severed parotid duct has been attempted in nine additional cases, bringing the total in the author's series to 12. There are eight proved successes, one presumptive success, two subcutaneous fistulas, and one obstruction at the anastomotic site with primary healing. The two fistulas have been relieved, one by spontaneous occlusion following non-operative management, and the other following operation aimed at occlusion of the duct.

An additional instance of subcutaneous fistula following unrecognized laceration of the duct has terminated in asymptomatic occlusion of the duct on non-operative management.

Technical modifications of the procedure of primary repair are discussed. Consideration is given to factors leading to failure of primary repair and to measures for dealing with ensuing salivary fistulas.

The author wishes to acknowledge his sincere gratitude to Drs. Jerry Stirman, William Thornton, Ben Wilson, Stanley Clayton, Joseph Cox, Leland Jackson, and other members of the Resident Surgical Staff of Parkland Hospital, Dallas, Texas. Without their earnest cooperation this study would not have been possible. They were

responsible for the recognition of cases, and in many instances, for the performance of the surgery.

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DISCUSSION.—DR. EDWARD M. HANRAHAN, Ruxton, Maryland: Doctor Sparkman's paper has reminded us of the great importance of immediate and serious care of damaging face injuries; if not properly treated at the time they give rise to grave difficulties later on. I refer of course to such injuries as those to the facial nerve, malar compound fractures, in addition to the injuries he just spoke of to the parotid duct. It would have been a great satisfaction to me to have heard this paper two weeks ago, and my discussion is prompted by an operation I had to perform about ten days ago on a 7-year-old child who, in the course of five weeks after a blow on the cheek, developed a tumor in this region about the size of an egg. Sialography was not accomplished because of obstruction of the duct. In exploring the tumor we went in by a peripheral approach and reflected a flap of cheek, came down on the tumor, and did an immediate biopsy, which was reported as sarcoma.

In dissecting out the tumor it was necessary to remove the buccal mucosa and the parotid duct as far back as its bifurcation in the gland, so we were left without a duct and with scant lining of the cheek. A one centimeter-wide flap of the buccal mucosa was sutured around an 18-gauge polythene tube in lieu of a catheter. The part of the duct made of mucosa measured perhaps one inch long, and we inserted the polythene tube through this, back into the larger bifurcation in the parotid gland. Suture was accomplished without much difficulty, although that part of the duct was small. We did not know how long to leave the tube in, but I felt at the time that the tube would act as a splint which would perhaps ensure healing to a greater extent by combating a certain amount of motion connected with the use of the masseter muscle and motions of the cheek. We did leave the tube in until it came out spontaneously about a week later.

It is altogether too early, of course, to speak of the end result in this case. The gland did not secrete a very liquid saliva; it was rather grumous material, and we felt it was important to ensure a passage through the reconstructed duct. I would like to ask Doctor Sparkman if he feels there is a particular advantage in removing the catheter early.

Dr. James D. Rives, New Orleans: I have been waiting for a good while to hear someone revive a very ancient method of handling fistulas, because of the limited experience I have had with it and the fact that it is so far in the past. Certainly, many of these cases are not repaired at the time of injury. Doctor Sparkman is to be congratulated on the delicate and accurate suture that he has done, and this method is certainly the best one to employ when the injury is fresh. When injuries of the salivary ducts are not repaired at the time of injury they develop pseudo-cysts with salivary fistulas.

There is a very old method for the correction of this condition, which I have had occasion to use three times with complete clinical success. It can be used on the parotid duct only when the injury is at or anterior to the border of the masseter muscle. The pseudo-cyst is opened and any foreign bodies present are removed. I have found fragments of glass on two occasions. A silk suture is passed through the floor of the cyst into the mouth. The other end of the suture is then threaded on the same or a similar needle and passed into the mouth in the same manner, at a point about one-fourth inch from the first puncture. This suture is then tied within the mouth very tightly so that it will cause necrosis. The loose ends are brought out through the corner of the mouth and taped to the cheek. This is simply to keep the patient from swallowing it. In two or three days this suture cuts through and produces an internal fistula instead of an external one.

In all three of my cases this simple procedure has resulted in closure of the fistula, and during a limited period of observation the internal fistula has persisted with complete relief of all symptoms. It may be that these fistulas have closed spontaneously at a later date with resultant atrophy of the gland. I found this procedure in Binnie's Operative Surgery, Seventh Edition; he attributed the procedure to Deguise.

Dr. James C. Owings, Baltimore: I would like to ask Doctor Sparkman whether he thinks it would be feasible to treat these glands with roentgen ray in rather heavy dosage, with the idea of cutting down the secretion or possibly knocking it out completely in the early stages. If it did work, it might make it unnecessary to do any operation in these cases. I do not know that it would be possible, but if it did knock out the secretion the duct would seal off and the gland would atrophy, which would be all that was necessary.

Dr. Robert S. Sparkman, Dallas, Texas (closing): I am very grateful for the discussion. Doctor Hanrahan mentioned the employment of a stent or, as it is frequently called, a dowel. The duct is so small that anything allowed to remain in it may occlude it. Such a dowel or stent was employed by seven of the eight authors who first described primary repair. In approximately half of the cases reported there was a transient salivary fistula. We have been fearful that a dowel, by occlusion, would do more harm than good.

The procedure of creation of an internal fistula by a cutting suture as mentioned by Doctor Rives was discussed by Morestin. In established fistulae of the duct he finally adopted ligation as the procedure of choice, after an extensive previous experience with attempted creation of an internal fistula. He felt that in most instances the internal fistula closed and the duct underwent occlusion by cicatrix.

In the manuscript it is stated that we have not attempted roentgen ray therapy, but have felt that it might be an effective means of bringing about occlusion of the duct or cessation of function of the gland. The only patient in this series to whom this procedure might have been applicable would have been the last patient, who underwent re-operation for a salivary collection. If a similar situation were encountered again where primary anastomosis was difficult, I think we would simply tie off the duct. If ligation failed to cure a fistula I would be inclined to resort to roentgen ray therapy.

URETERAL TUMORS*

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URETERAL TUMORS, though infrequently encountered, are not as rare as the small number of published cases indicates. Recently a growing consciousness of these tumors and improvement in diagnostic methods have resulted in a relatively large number of reported cases. The object of this paper is to report seven additional cases.

The clinical material reported in this paper is derived from the records of 6000 consecutive patients who have been examined during the past 12 years because of urinary symptoms. There were 157 patients in whom one or more neoplasms of the urinary tract were encountered and in seven of these the neoplasm involved the ureter.

TABLE I.—*Neoplasms.*

Tumor of Renal Cortex	27
Tumor of Renal Pelvis	6
Tumor of Ureter	7
Tumor of Bladder	109
Tumor of Urethra	8

CASE REPORTS

Case 1.—(No. 2825). A 64-year-old mother of three children developed pain in the left side and gross hematuria 15 months before admission. From the onset pain and hematuria recurred at increasingly shorter intervals and during the last three months preceding admission had been continuous. She had lost 8 pounds.

Cystoscopy at the first examination, February 9, 1944, revealed a large papillary tumor involving the left lateral wall of the bladder and the left ureteral orifice. The right ureteral orifice was normal. The left ureteral orifice could not be identified.

The tumor was thought to be a transitional cell papilloma of the bladder exhibiting little evidence of malignancy (Grade I), and this view was confirmed by microscopic examination of a portion of the tumor which was removed through the cystoscope. Roentgenograms after intravenous diodrast revealed a normal right pelvis and ureter. The left pelvis and ureter were not visible. Although tumor of the left kidney could not be excluded, it was clear that the vesical end of the ureter had been involved by tumor to such an extent that it was no longer patent. Ureteral obstruction seemed the obvious explanation of the pain and roentgen ray findings of the left kidney.

On February 22, 1944, the bladder was opened. The main tumor mass, together with some of the bladder wall, was excised. A few small papillary tumors on or near the trigone were destroyed by electrocoagulation. The wounds healed rapidly and she was discharged on March 5, 1944. On 10 occasions during the first 18 months following operation, one or more tumors were found growing in various parts of the bladder. These recurrences were destroyed by electrocoagulation. Pain in the left side became

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more severe and in October, 1945, she finally consented to the removal of the left kidney and ureter.

On October 24, 1945, a two-stage nephro-ureterectomy was begun by removing the kidney and the upper half of the ureter. The upper end of the distal segment of the ureter was mobilized and brought to the surface through a stab wound. During this surgical procedure a mass was palpated in the ureter at the level of the iliac vessels. Both the kidney and the excised portion of the ureter were enormously dilated but in neither was there a tumor.

On November 3, 1945, the remaining portion of the left ureter and the adjacent bladder wall were excised. The ureter was distended by a mass which extended from the level of the iliac vessels to the bladder wall. Histologically the tumor was a transitional cell papillary carcinoma (Grade II), similar in many respects to the bladder tumor excised 21 months previously. Following operation she developed phlebitis of the veins of the lower extremity, which subsided rapidly. She was discharged on November 22, 1945.

The patient remained well until June 16, 1947, when she returned because of pain in the left hip and back. At this time a small tumor was found in the bladder and destroyed by electrocoagulation. Roentgen ray examination of the chest revealed "a little pleural thickening in the left base." Roentgenograms of the lumbar spine, pelvis and hips showed no bone lesions. The patient was not seen again, but it is known that she gradually lost weight and strength and died on October 31, 1947, presumably because of the neoplasm.

Case 2.—(No. 3782), age 64. He developed painless and persistent hematuria 10 days before admission date.

When first examined on October 9, 1945, the cystoscopic findings were as follows: The bladder was normal. Both ureteral orifices were normal. The right orifice emitted clear urine; the left orifice, bloody urine. Both ureters were catheterized without difficulty. A roentgen ray film of the urinary tract did not show a stone. Indigo carmine was excreted normally by the right kidney. The dye was not excreted by the left kidney at any time during the course of the cystoscopy. Pyelography revealed a normal pelvis and ureter on the right side. There was a very large hydronephrosis on the left side. The left ureter was sharply angulated a little below the ureteropelvic junction and the segment between these two points did not fill. The distal portion of the ureter was dilated in the upper two-thirds and filled in an irregular mottled fashion. These findings strongly suggested tumor of the left ureter probably at the ureteropelvic junction. Removal of the left kidney and ureter was advised.

On October 15, 1945, the first part of a two-stage nephroureterectomy was performed by removing the left kidney and the upper end of the ureter. In the course of the operation no tumor could be palpated in the renal pelvis or in the upper one-half of the ureter. On careful examination of the specimen removed at operation no evidence of tumor was found. The diagnosis of ureteral tumor thus became questionable, and it was decided to delay the second stage of the operation to permit further study of the left ureter. The patient suffered no complication and was discharged on October 26, 1945.

He was again cystoscoped on November 19, 1945, because he had noted hematuria on two occasions during that month. At this time the bladder was normal. The ureteral orifices were normal and the urine grossly clear. Retrograde pyelography demonstrated a normal right pelvis and ureter. On the left there was a ureteral filling defect which extended upward from the bladder wall about 2 inches in the ureterogram (Fig. 1). The patient was advised to have the remaining part of the left ureter removed, and in January, 1946, this was accomplished. Examination of the excised specimen revealed a papillary tumor involving the distalmost 2 inches of the ureter. Histologically the tumor proved to be a papillary carcinoma.

The patient remains asymptomatic now 44 months after operation.

Case 3.—(No. 4460), age 70. This patient suffered from severe heart disease for several years. One month ago he was admitted to the hospital with cardiac decompensation and recompensated. One week later he developed severe left-sided renal colic and gross hematuria with clots. The pain and hematuria persisted. When first seen on January 8, 1947, the cystoscopic findings were as follows.

The bladder and both ureteral orifices were normal. The right ureter emitted clear urine; the left, bloody urine. The excretion of indigo carmine by the right kidney was normal. The amount excreted by the left kidney could not be estimated because of decreased renal function and much blood in the urine. In the plain film there were many shadows in the right upper quadrant thought to be gallstones. The left kidney outline appeared normal in size, shape and position. The outline of the right kidney was obscured by gas in the intestinal tract. There was calcification of the right sacrosciatic ligament. Retrograde pyelography revealed normal filling on the right side. On the left side the pelvis and lower calyx were dilated (Fig. 2). The upper half of the left ureter was dilated. The remainder of the ureter was not filled. In both the left renal pelvis and in the dilated upper ureter there were irregular, mottled filling defects. On January 10, 1947, intravenous pyelo-ureterograms after diodrast failed to outline the left kidney pelvis 40 minutes after administration of diodrast. There was normal concentration and filling on the right side. On January 13 retrograde pyelograms made on the left side showed that one filling defect persisted in the lower major calyx (Fig. 3). Other filling defects had disappeared in the upper major calyx and there was moderate hydronephrosis present. There was considerable irregularity of the ureter in both its proximal and distal thirds and some dilatation in the middle third. The findings were suggestive of carcinoma arising from the renal pelvis with implants in the ureter. On January seventeenth the left kidney and the upper third of the left ureter were removed. The distal segment of the ureter was freed down to the iliac vessels and brought to the surface through a stab wound in the abdominal wall.

Examination of the specimen removed at operation disclosed only one tumor, a transitional cell papillary carcinoma involving the inferior major calyx. The patient's convalescence was satisfactory except that the wound disrupted for a distance of 5 inches. The wound was secondarily closed January 31, 1947. The patient was discharged on February 4, 1947.

He continued to improve and gained in weight. The urine remained clear. Cystoscopic examination on May 14, 1947, revealed that the bladder and both ureteral orifices were normal. The patient declined to have the lower segment of the ureter removed. On August 11, 1947, he noted blood in the urine.

Nine days later he re-entered the hospital and cystoscopic examination of the bladder disclosed a tumor protruding from the left ureteral orifice. On August 28, 1947, the lower segment of the left ureter including a margin of the bladder wall was excised. Examination of this specimen revealed a tumor growing in the distal two inches of the ureter. Microscopically this tumor was a transitional cell papillary carcinoma. Recovery was uneventful and he was discharged September 7, 1947. One month later the bladder was inspected and found normal. On February 24, 1948, three small papillary tumors were found in the bladder growing from widely separated localities. After biopsy these were destroyed by electrocoagulation. Histologically they were similar to the tumors which had been found first in the renal pelvis and later in the ureter. Tumors were again found in the bladder on April 15, 1948, and destroyed by electrocoagulation. On August 25, 1948, he again passed bloody urine. A papillary tumor was present on the posterior bladder wall which appeared to have infiltrated the underlying tissues. At this time a roentgen ray film of the chest revealed "marked elevation of the right leaf of the diaphragm with a small amount of fluid in the left pleural cavity. There was minimal pleural thickening in the left costophrenic angle. A small area of increased density was observed in the right costophrenic angle, the nature of which was not quite

FIG. 1 FIG. 2

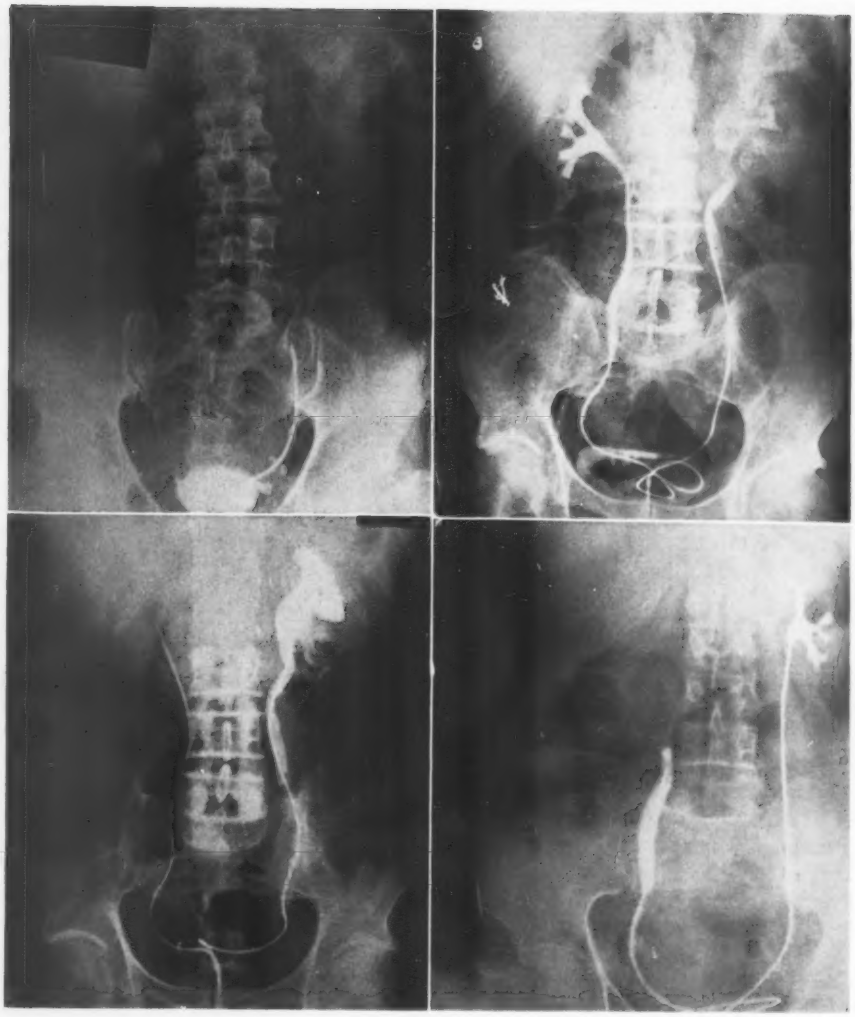

FIG. 3 FIG. 4

FIG. 1.—Ureterogram showing filling defect in the lower end of left ureter.

FIG. 2.—Pyelo-ureterogram showing irregular mottled defects in dilated lower calyx and pelvis of left kidney and upper end of the corresponding ureter.

FIG. 3.—Same as Figure 2. Left pyelo-ureterogram made five days later showing a single constant defect in lower calyx of left kidney and a dilated upper segment of left ureter ending irregularly and suggesting a second tumor (transplant) at that point.

FIG. 4.—Ureterogram showing two filling defects in the right ureter, the upper lesion producing obstruction.

clear, but it was thought probably to be atelectasis. A marked localized dilatation of the descending portion of the aorta compressed the left main bronchus. Impression—aneurysm of the descending aorta." The following day the right chest was aspirated and 1000 cc. of fluid withdrawn. Cancer cells were found in a cell block prepared from this fluid. The character of these cells suggested a glandular tumor originating in the lung and unrelated to the papillary tumor in the urinary tract. A roentgen ray film made after aspirating the chest was interpreted as follows: What was originally thought due to an elevated diaphragm was due to fluid. The medial portion of the right lung base was almost uniformly opaque. Findings were probably due to metastatic disease associated with atelectasis. He continued to grow worse, and died on September 10, 1948. Autopsy not obtainable.

Case 4.—(No. 5259). A 75-year-old mother of 10 children stated that 10 years ago she had had a severe attack of renal colic associated with gross hematuria. Two years ago she had had a similar attack. The patient was told she was passing a kidney stone. Three weeks ago she developed soreness in the right loin and lumbar region. There were laborlike pains in the lower abdomen. These symptoms had persisted. She had never passed a stone.

At the first examination on May 17, 1948, the cystoscopic findings were as follows: The bladder and both ureteral orifices were normal. The left ureter was catheterized without obstruction. On the right side the catheter met obstruction about 16 cm. above the bladder. The urine from the bladder contained a trace of albumin and 25 red blood cells per high power field uncentrifuged urine. The catheter on the right side did not drain. The urine from the left kidney was normal. Indigo carmine was normally excreted by the left kidney. A K. U. B. film did not show a shadow which could be interpreted as a calculus. Retrograde pyelograms revealed a normal pelvis and ureter on the left side. On the right side the ureter filled to a point about 5 cm. below the uretero-pelvic junction where there appeared to be complete occlusion of the ureter by an irregular mass (Fig. 4). From this point downward the ureter was dilated, the dilatation terminating in another filling defect 2½ cm. long at the level of the iliac vessels. The remainder of the ureter was normal. Diagnosis: multiple tumors of the right ureter.

On May 22, 1948, the right kidney and ureter were removed in a one-stage operation after the tumor in the upper third of the ureter had been explored and found to be a transitional cell papillary carcinoma. The ureter was divided and ligated about one inch above the bladder which was left intact. The patient made a satisfactory recovery. An examination of the specimen removed at operation revealed two transitional cell carcinomas of the ureter, one just below the uretero-pelvic junction and the other at the junction of its middle and lower third. The renal pelvis was slightly dilated but no tumor was present. The patient had an uncomplicated convalescence and was discharged on May 31, 1948. She has had no further trouble to date.

Case 5.—(No. 3222), age 75, stated that 5 years ago, on November 4, 1944, his right kidney was removed for a tumor of the renal pelvis which proved to be a papillary adenocarcinoma Grade II (Fig. 5). The right ureter was not removed. Since that time he had enjoyed good health until the onset of painless hematuria 2 weeks ago. The hematuria has persisted.

At the first examination July 5, 1949, the cystoscopic findings were as follows: The bladder and both ureteral orifices were normal. The right orifice was immobile; the left orifice emitted grossly bloody urine. The left ureter was catheterized without obstruction. The right ureter was also catheterized but the ureter was obstructed 12 cm. above the bladder. The urine from the bladder was grossly bloody. Urine from the left kidney: pus O; red blood cells 350; casts O. Culture: few colonies of *B. coli*. K. U. B. film was negative for stone. Retrograde pyelo-ureterogram on the left side

revealed normal filling of the pelvis and ureter. On the right side a ureterogram revealed many irregular filling defects; the right kidney was absent and there was some extravasation of the media from the ureteral stump into the retroperitoneal tissue (Fig. 6). Diagnosis: multiple tumors right ureter; idiopathic hematuria left kidney. At the present time the patient's general health is satisfactory and efforts are being made to stop the bleeding from the left kidney.

Case 6.—(No. 5924). A 33-year-old mother of 2 children stated that 5 years previously she had developed severe left-sided renal colic. The pain was associated with frequency, urgency and gross hematuria. The attack lasted several days, during which she had chills and fever. She continued to have similar attacks but had never passed a

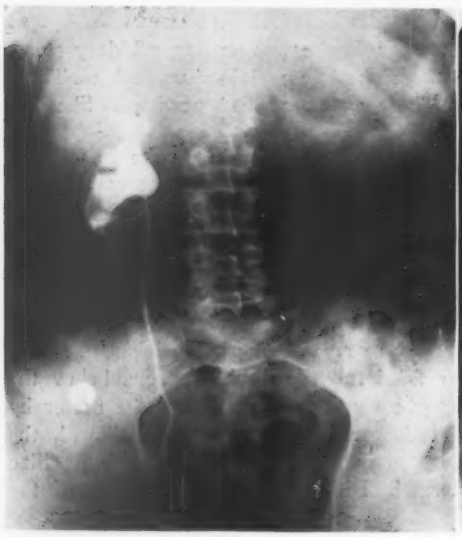

FIG. 5

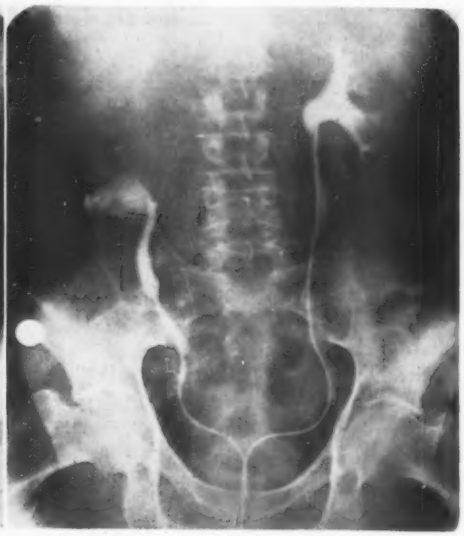

FIG. 6

FIG. 5.—Pyelogram showing defect in lower calyx of the right kidney.

FIG. 6.—Same case as Figure 5. Ureterogram made five years later showing multiple filling defects in right ureter and extravasation of media through its stump which was left at nephrectomy in 1944.

stone. Three years ago she consulted a urologist, who found a papillary tumor growing in the left ureteral orifice. The right ureteral orifice was normal. Both ureters were catheterized without obstruction. A roentgen ray film of the urinary tract showed no evidence of stone. Retrograde pyelograms revealed a small hydronephrosis on the left side. The left ureter was dilated throughout its course. The right pelvis and ureter were normal. The bladder tumor was destroyed by electrocoagulation without biopsy. Following this the patient remained in good health for three years. In the latter part of May, 1949, she redeveloped left-sided pain associated with frequency, dysuria and gross hematuria. These attacks became progressively worse.

On admission to the hospital July 12, 1949, the cystoscopic findings were as follows: The bladder and right ureteral orifice were normal. The left ureteral orifice was dilated 4 plus. On continued observation a tumor mass was seen to protrude through the dilated left orifice during ureteral contraction and to recede out of sight through it during the

interval of relaxation. Both ureters were catheterized without obstruction. A K. U. B. film showed no evidence of stone. Retrograde urograms were interpreted as follows: On the left side there was a small hydronephrosis. The left ureter was dilated principally in its lower third where there was an irregular filling defect about 6 cm. in length (Fig. 7). The right kidney and ureter were normal. Diagnosis: tumor of the lower third of the left ureter. On July 18, 1949, the left kidney and ureter were removed in a one-stage operation. When the specimen was examined postoperatively the tumor was found to be a large polypoid mass filling the terminal 7 cm. of the ureter (Fig. 8). The tumor was nourished by a long slender pedicle which attached itself to ureteral mucosa about 4 cm. below the level of the iliac vessels. Except for the pedicle the mass was entirely free. Histologically the tumor was a benign polyp. The patient made a satisfactory recovery and was discharged from the hospital July 31, 1949.

Case 7.—(No. 3745). A male, age 63, was admitted July 27, 1949, because of a severe attack of coronary occlusion from which he died within a few hours.

The patient had consulted an urologist in August 1945, 2 days after the onset of painless hematuria. He was found to have a papillary tumor springing from the left wall of the bladder a short distance from the ureteral orifice. On September 11, 1945, the tumor was destroyed transurethrally by electrocoagulation after a piece of the tumor had been removed for microscopic study. Histologically the tumor was classified as a papillary carcinoma. On October 18, 1949, a small area of tumor persisted at the site of the original growth and this was treated by electrocoagulation. He had had no further trouble during the 4 years preceding his death.

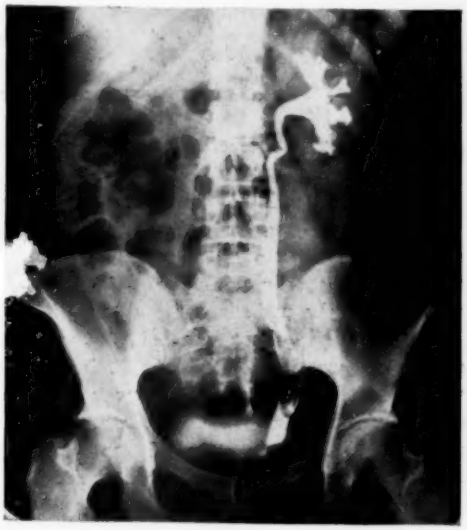

FIG. 7.—Left pyelo-ureterogram showing filling defect in lower end of ureter.

At postmortem examination the findings were as follows: A soft papillary tumor some 2 cm. in diameter surrounded the orifice of the left ureter. The lesion was somewhat hemorrhagic and was rather friable. Microscopically it was composed of frond-like stalks of well-differentiated transitional epithelium supported on thin connective tissue cores. Sections through the base showed the tumor to be confined to the surface tissues of the bladder. No evidence of invasion could be found. The absence of cytologic changes suggesting malignancy and the failure to demonstrate any invasion of the bladder wall made me diagnose this lesion as a benign one. In the right ureter about 6 cm. above the bladder two small papillary growths protruded into the lumen. Each of these lesions arose from a narrow pedicle and grossly appeared to involve only the surface epithelium. Microscopic examination confirmed the absence of invasion and revealed the epithelial cells to be mature in type. On the basis of histological findings these tumors also were classified as benign.

DISCUSSION

The bladder and renal cortex gave rise to 86.5 per cent of all tumors found in the urinary tract. Only 8.4 per cent were found in the renal pelvis and

ureter. Numerically, pelvic and ureteral tumors were about equal (Table I). In the ureter malignant tumors predominated.

TABLE II.—*Ureteral Tumors.*

Case	
1.	Transitional cell papillary carcinoma
2.	Transitional cell papillary carcinoma
3.	Transitional cell papillary carcinoma
4.	Transitional cell papillary carcinoma
5.	Transitional cell papillary carcinoma
6.	Benign polyp
7.	Benign papilloma

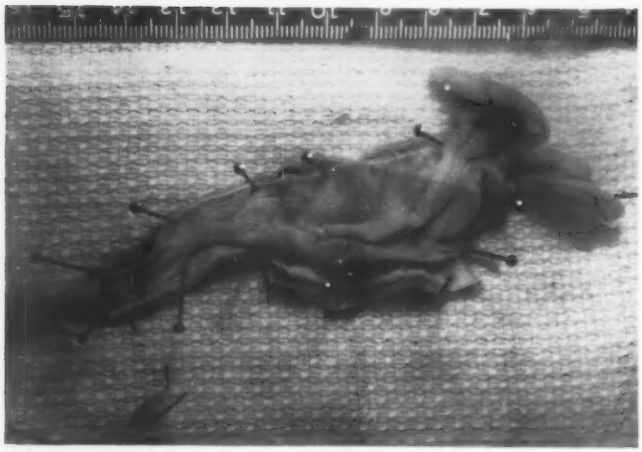

FIG. 8.—Photograph of lumen of left ureter showing the tumor.

Transitional cell papillary carcinoma was the only type of malignant tumor found in the ureter. These tumors did not readily invade normal tissue or metastasize to other structures. In one case more than one tumor was present in the same ureter. These tumors were always unilateral.

Multiple tumors in the ureter are explained by two theories. One is on the basis of cells transplanted from a parent growth. The other holds that the same cytologic changes which produced one tumor, by virtue of wide dissemination, produced all tumors. This latter view better explains the papillary carcinoma (Case 5), which developed in a ureteral stump 5 years after the corresponding kidney had been removed for a similar tumor in the renal pelvis. A wider experience with epithelial growths in the bladder favors the conclusion that many papillary tumors in the beginning are benign. Multiplicity is no evidence of malignancy. However, cellular changes in these tumors are towards cancer and eventually they become malignant.

Tumors of the ureter were associated with gross hematuria and pain in the side and back, which at times attained the intensity of renal colic. Fre-

quency of urination was infrequent. Dysuria occurred during the passage of clots. Hematuria was more profuse and persistent than ordinarily results from renal calculus. Stone was thought to be the cause of symptoms in 3 patients. In no case was there a palpable mass or any other clinical evidence of cancer. On clinical symptoms alone ureteral tumor was considered a possibility in only the first case. The preoperative diagnosis of ureteral tumor was made entirely upon indirect and direct evidence found in the urograms. Indirect evidence was the absence of stone, frequently a surprise, and dilatation of the renal pelvis and a proximal segment of the ureter. Direct evidence was a filling defect in the ureter at the distal end of the dilated segment. In Case No. 4 a duplicating lesion produced a second defect at a higher level in the dilated segment. Blood clots often obscured the defect of the tumor and produced others which were misleading. In such cases it was found advantageous to test the constancy of suspicious shadows by repeating the urograms. Cases Nos. 1 and 6 are examples of error in accepting an obvious tumor in the bladder as a complete diagnosis.

Five patients were treated by nephro-ureterectomy which was performed in one or two stages.

TABLE III.—*Operations.*

Case	
1.	Two stage nephro-ureterectomy
2.	Two stage nephro-ureterectomy
3.	Two stage nephro-ureterectomy
4.	One stage nephro-ureterectomy
5.	Operation considered inadvisable
6.	One stage nephro-ureterectomy
7.	Diagnosed at postmortem

The operation was in each case carried out from above downward, first the kidney and last the ureter was removed.

RESULTS

There were no operative deaths. Two of the 5 patients who were treated surgically, patients in Cases 1 and 3, are dead. Patient in Case 1 survived two years and died of metastasis. Patient in Case 3 lived one year and died of cardiovascular disease after developing a primary carcinoma of the lung. Three patients have remained well, an average of 18 postoperative months.

In the first 3 cases nephro-ureterectomy was performed in two stages because it was thought that the risk of the operation would be less if done in that way. In practice, however, the ureter is most easily removed with the kidney, and little additional time is then required to extirpate it. There was no experience in this group of cases which indicated the risk of nephro-ureterectomy would be reduced by performing it in two stages. The one stage operation was employed in the last 2 cases treated surgically (Cases 4 and 6).

The data obtained from the records of 5 patients who had transitional cell papillary carcinoma of the ureter show that in 2 of them the corresponding

kidney had been removed for a similar tumor in the pelvis. In Case 4 a tumor was probably present in the lower end of the ureter when the kidney was removed. At that time the ureter was dilated except for its terminal 5 cm. where a tumor was subsequently found. In Case 5 the ureter was apparently normal when the kidney was removed and a tumor was not found in it until five years later.

In cases of papillary carcinoma of the renal pelvis the corresponding ureter is predisposed to develop similar tumors. If we expect to improve the results of surgical treatment of papillary tumors of the renal pelvis both the kidney and ureter must be removed. In this way a number of ureteral tumors will be prevented and the incidence of bladder tumors minimized.

An analysis of these 7 cases raises two points which reflect on the advisability of routinely performing the operation in the manner described: First, the majority of the tumors were situated in the lower end of the ureter and in 2 of the 7 patients the tumors were found to be benign. For these reasons it would seem better to begin the operation below by exposing the ureter and exploring the tumor. Frozen sections could be employed to establish the nature of doubtful lesions. In Case 6 the polyp could have been easily removed and the ureter left intact. In Case 7 the lower end of the ureter, including both benign papilloma and a rim of bladder wall, was subject to excision and the defect to repair by ureterovesical anastomosis.

The value of treating tumors limited to the distal end of the ureter by segmental resection and ureterovesical anastomosis can not at present be appraised. There is much evidence that papillary tumors, benign or malignant, are disposed to grow at lower levels in the urinary tract. While a tumor in the renal pelvis is frequently associated with or followed by similar tumors in the ureter and finally in the bladder, there is no evidence that this trend is ever reversed. Furthermore, primary ureteral tumors are low in the scale of malignancy and if subsequent tumors grow in the remaining portion of the ureter or renal pelvis their recognition and removal before metastasis occurs is quite probable. Careful and prolonged postoperative observation is essential for patients treated by segmental resections for primary ureteral tumors.

SUMMARY

1. Seven cases of ureteral tumors which were found in a group of 6000 patients with urinary symptoms are reported.

2. These tumors are compared with tumors found elsewhere in the urinary tract in the same group of patients.

3. The diagnosis, clinical behavior and treatment of the seven ureteral tumors are discussed.

4. In papillary carcinoma of the renal pelvis the ureter should be removed with the kidney.

5. The treatment of tumors in the distal end of the ureter by segmental resection and ureterovesical anastomosis has obvious advantages over nephroureterectomy.

CALCIFIED CYST OF THE SPLEEN

WITH PRELIMINARY REPORT OF EXPERIMENTAL OCCLUSION OF THE BLOOD SUPPLY OF THE SPLEEN*

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CYSTS OF THE SPLEEN are rare and are the least frequently encountered cystic disease involving abdominal viscera. Pemberton[1] reported 800 cases in which splenectomy was performed, and noted that only 0.5 per cent showed evidences of cyst formation. The first reported case of cystic disease of the spleen is credited to Andral in 1829,[2] and Harmer and Chalmers[3] collected reports of 162 cases from the literature through 1944. Since then, 21 additional cases have been reported, thus bringing the total to 183. Fowler,[4] as early as 1913, summarized the pathologic findings of this disease and advanced the accepted theories of the etiology and the classification of splenic cysts.

Other classifications have been proposed, but Fowler's remains the most inclusive and useful. He divides splenic cysts into dermoid, parasitic, and non-parasitic types.

Dermoid cysts are extremely rare and are not considered in this report. The parasitic form is associated entirely with echinococcic disease. The non-parasitic class is divided into true and pseudo cysts, which are distinguished by the presence or absence of a specific secreting lining. The true cysts include: first, the infoliation type, which may be associated with either inflammation or trauma; second, the dilatation type, or polycystic lesions; and third, the neoplastic type, such as hemangioma and lymphangioma. Pseudo cysts are thought to result from trauma with hematoma formation and later degeneration, or from infarction with subsequent necrosis. Most cysts are of the non-parasitic type, with which this report is concerned.

Many theories have been advanced as to the cause of non-parasitic splenic cysts,[3, 5] but trauma is the only proved significant factor. In order for these cysts to form, the trauma must be sufficient to rupture or otherwise damage the splenic parenchyma, so that a hematoma will be produced which will later degenerate. Infoliation cysts, moreover, are thought to develop following traumatic rupture of the splenic capsule with infolding of the peritoneum. These infoldings become enclosed by the surrounding parenchyma, thus forming cavities having a peritoneal-like lining.[5] Trauma, however, may not

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be essential for the production of these infoldings. Pepere[6] suggested that serous cysts originate from cellular rests formed under the splenic capsule by abnormal invagination of the perisplenium during fetal development. These cellular residues may disappear, but may later give rise to small subcapsular cysts.

Inflammation cannot be underestimated in the production of lienal cysts. The role of lymph stasis is admittedly difficult to evaluate, since it does not provide an adequate explanation of the origin of polycystic disease of the spleen. The infarction theory of splenic cyst formation has likewise been advanced without adequate clinical or experimental evidence.

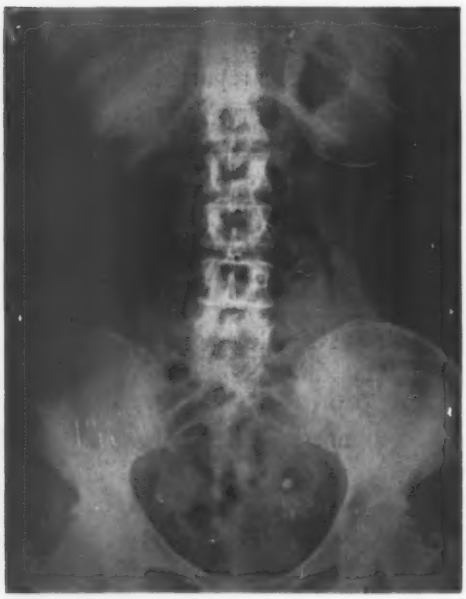


FIG. 1A

FIG. 1.—(A) Roentgenogram of patient showing calcified cyst in left upper quadrant of abdomen.

Since an enlarged spleen is vulnerable to trauma, it is easy to understand the relative frequency with which a splenic cyst is found in patients with antecedent splenomegaly. The spleen is known to enlarge during menstruation and pregnancy,[7] and it is this factor which is believed to be responsible for the high incidence of splenic cysts in women of childbearing age. A history of trauma, it should be noted, cannot always be considered reliable, since most individuals can recall injuries to the abdomen of variable degree.

Cysts of the spleen usually cause no symptoms, and when they are small, usually are found incidentally.[8] Large cysts usually produce pressure, and pain is the predominant symptom. This may be expressed as a feeling of heaviness in the left hypochondrium, but if there is associated peritoneal involvement there may be severe pain with vomiting and fever. Digestive disturbances have been observed as a result of displacement of the stomach and intestines. Dyspnea and circulatory embarrassments rarely occur.

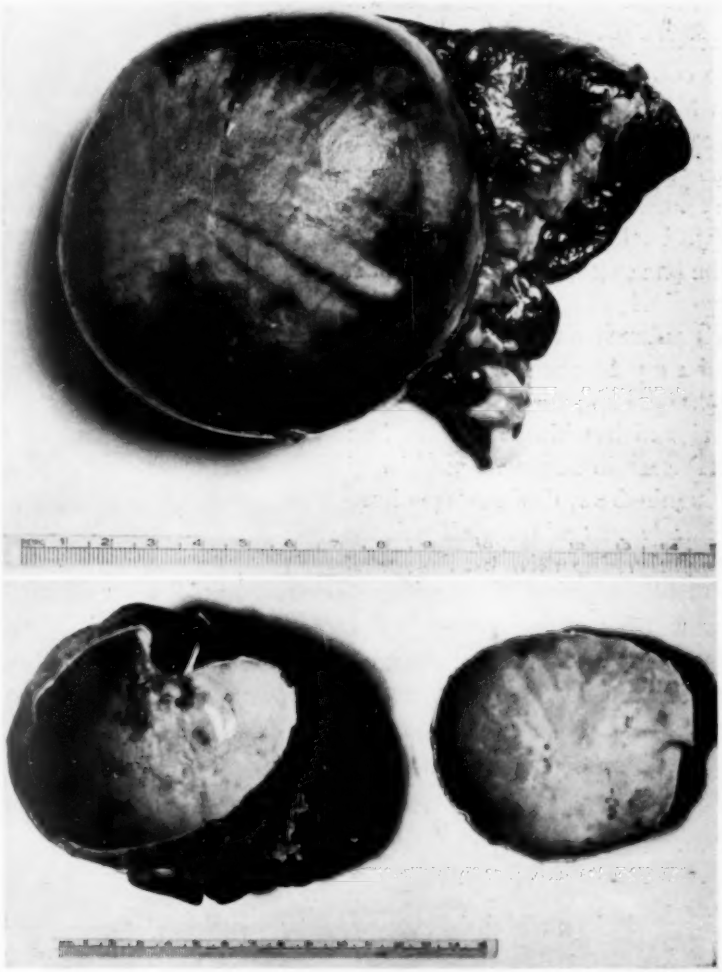
The ease of diagnosis is in direct proportion to the size of the cyst. Small cysts usually escape detection, while large cysts frequently are suggested by left upper quadrant pain and mass. Roentgen observations of splenic enlargement show displacement of the stomach and intestines to the right and downward. The left kidney also may be forced downward. In the absence of calcification, a definite preoperative diagnosis of splenic cyst can infrequently be made. Sweet,[9] however, states that with large cysts, the diagnosis can readily be made. In diagnosis, consideration should be given to other causes of splenic

enlargement, and cysts of the spleen must be differentiated from those of the mesentery, omentum, pancreas, kidney, and left lobe of the liver.

Careful hemotologic investigation cannot be overemphasized. This should include complete bone marrow and peripheral blood studies. Pneumoperitoneum[10] may be utilized in addition to the usual radioscopic examinations of gastro-intestinal and genito-urinary tracts.

Calcification of an aneurysm involving the splenic or renal artery may produce roentgen ray evidence not unlike that of a calcified cyst of the

B



C

FIG. 1.—(B) Gross specimen of the removed spleen with the calcified cyst occupying the greater portion of the lower half of the spleen. (C) A section through the calcified cyst showing the thickness and the general appearance of the cyst cavity.

spleen. Kierulf[11] states that in an aneurysm the large ring of calcification is broken. The expansile pulsation and bruit may be the differentiating characteristics. Calcification of the splenic artery may be found in advanced arteriosclerosis. The vessel may have a continuous outline or there may be a break in its continuity.

Leader and Goldberg[12] have demonstrated the similarity of calcified cysts of the liver to those of the spleen. They have shown that the echinococcus cyst of the liver may frequently be calcified. The inability to distinguish the spleen from the left lobe of the liver may make the diagnosis more difficult.

In the early reports on treatment of cysts of the spleen, marsupialization was the method of choice. As the knowledge of the disease and a positive

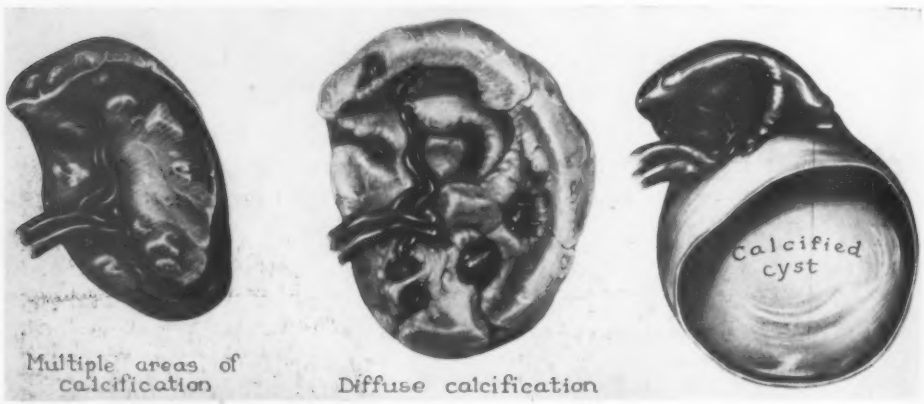


FIG. 2.—Drawing representing various types of calcification involving the spleen.

approach to the surgical phase of treatment advanced, removal of the spleen has become universally accepted. Splenectomy, however, is recommended only after every effort has been made to determine preoperatively the exact nature of the lesion. The results from splenectomy in the treatment of cysts have been good, with an operative mortality of 4 per cent.[5] The morbidity and mortality have been consistently reduced in the more recent reports.

There have been only 30 reported calcified cysts of the spleen.[13-41] The cause of calcification of these cysts is not known. The report which follows describes a case of such a condition.

CASE REPORT

Mrs. R. B. B., 66 years old, white, was admitted to Emory University Hospital on February 6, 1949, with a history of recurrent moderate pain in the left upper quadrant of the abdomen of nine months' duration. She had first been seen in November, 1948, and stated that her pain had been gradually increasing in severity. Past and family history were non-contributory. At time of admission, she was well developed and

TABLE I.—*Experiment A.*

TABLE I EXPERIMENT A

DOG	PROCEDURE	GROSS FINDINGS OF SPLEEN (14TH. DAY)
501	LIGATION OF SPLENIC ARTERY	1. DECREASE IN SIZE 2. PERISPLENITIS 3. SEVERAL SMALL INFARCTS
502	LIGATION & DIVISION OF SPLENIC ARTERY	1. NO CHANGE IN SIZE 2. PERISPLENITIS 3. NO INFARCTS NOTED
503	SAME AS ABOVE	1. MODERATE DECREASE IN SIZE 2. OMENTUM ADHERENT 3. THREE LARGE INFARTS
504	SAME AS ABOVE	1. NO CHANGE IN SIZE 2. SEVERAL SMALL INFARTS

FIG. 3

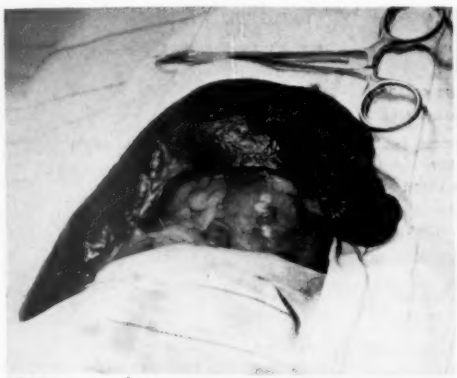


FIG. 4

FIG. 5

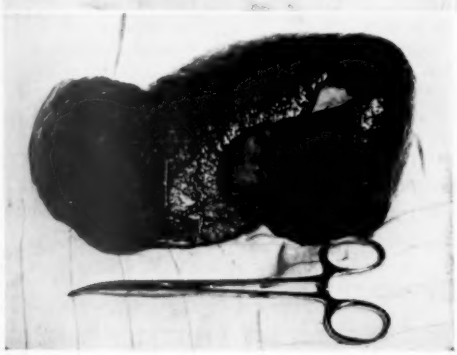


FIG. 3.—Photograph of the spleen of a dog 14 days after ligation of the splenic artery, demonstrating areas of infarction and perisplenitis.

FIG. 4.—Spleen of a dog 39 days after ligation and division of the splenic artery and the vessels of the gastro-lienal ligament, demonstrating marked atrophy with adherent omentum and few scattered areas of infarction.

FIG. 5.—Spleen of a dog 37 days after torsion of the entire splenic pedicle through 360 degrees and a constriction of the pedicle with a ligature over a polythene band. There is a marked increase in size with a perisplenitis and numerous small infarcts.

nourished and in no apparent distress. The physical examination was negative except for the left upper quadrant of the abdomen, where a mass extending 4 cm. below the costal border was palpable. A roentgenogram showed an ovoid mass 9 cm. in diameter which was surrounded by a rim of calcium.

At operation, the spleen was found to be enlarged to about twice its normal size. The lower portion of the organ was occupied by a 9 cm. cyst with a yellowish-brown, calcified wall. Splenectomy was performed, and the patient had a normal convalescence and has had no further complaints.

Gross pathologic examination revealed a spleen which was divided roughly into two portions. One was about the size of a normal spleen made up of dark red pulp containing numerous large white areas. The entire organ was more firm than usual. The lower end was occupied by a cyst, the surface of which was extremely dense and appeared to be calcified. The wall was 2 mm. thick, and the inside was covered with a smooth membrane. The cyst was filled with about 300 cc. of yellowish opalescent fluid containing numerous cholesterol-like crystals.

TABLE II.—*Experiment B.*

			PATHOLOGY OF SPLEEN		
DOG	PROCEDURE	P.O. DAY	GROSS	MICROSCOPIC	RESULT
501	LIGATION & DIVISION	70	1. NO CHANGE IN SIZE 2. FIRM 3. SLATE-BLUE IN COLOR 4. SEVERAL SMALL INFARCTS	PERISPLENITIS	ALIVE
502	SAME AS ABOVE	39	1. MARKED DECREASE IN SIZE 2. SOFT & SPONGY 3. DARK RED IN COLOR 4. OMENTUM ADHERENT 5. FEW SMALL INFARCTS	INFARCTION PERISPLENITIS ATROPHY	ACCIDENTAL DEATH
503	SAME AS ABOVE	65	1. MARKED DECREASE IN SIZE 2. FIRM 3. DARK RED IN COLOR 4. OMENTUM ADHERENT	INFARCTION PERISPLENITIS ATROPHY	ALIVE
504	LIGATION & DIVISION OF SPLENIC ARTERY & GASTRO-LIENAL LIGAMENT	24	1. MARKED DECREASE IN SIZE 2. SOFT & SPONGY 3. REDDISH-BROWN IN COLOR 4. PERISPLENIC ABSCESS 5. SEVERAL LARGE INFARCTS 6. OMENTUM ADHERENT	INFARCTION PERISPLENIC ABSCESS ATROPHY	AUTOPSY FINDINGS— PNEUMONIA, LOCALIZED PERITONITIS WITH PERISPLENIC ABSCESS

The microscopic findings of the upper portion of the spleen were normal. The cyst wall consisted of fibrous tissue with no evidence of an epithelial lining. Early calcification was found in the fibrotic wall, and normal splenic tissue was identified on the outer periphery. Echinococcus organisms were not seen.

PRELIMINARY RESULTS OF EXPERIMENTAL STUDY

It has been previously mentioned that there are many theories of splenic cyst formation,[8, 10] but supportive experimental evidence is lacking. The following experiments were designed using mongrel dogs to study the effects on the spleen of varying degrees of occlusion of the splenic blood supply.

The blood vessels supplying the spleen were occluded in part or totally either by ligation and division of the arteries in the pedicle and gastro-lienal ligament or by torsion of the pedicle and gastro-lienal ligament or by a com-

bination of the two procedures. The spleens were re-examined at varying intervals, and biopsies of regions showing gross change were obtained. The extent of vascular occlusion and the resulting gross and microscopic changes in the spleen are summarized in the accompanying tables.

It was found that after the splenic artery alone is ligated, collateral circulation of the spleen in dogs is sufficient to maintain normal splenic architecture.

Following occlusion of the arteries in the splenic pedicle and gastro-lienal ligament, infarcts develop, usually with a decrease in size of the spleen Collateral circulation develops to a variable extent through the vessels in the greater omentum, the gastro-lienal, and lieno-renal ligaments.

TABLE III.—*Experiment C.*

			PATHOLOGY OF SPLEEN		
DOG	PROCEDURE	P.O. DAY	GROSS	MICROSCOPIC	RESULT
505	TORSION OF THE SPLENIC PEDICLE & GASTRO-LIENAL LIGAMENT (720°)	34	1. MARKED DECREASE IN SIZE 2. SOFT 3. REDDISH-BROWN IN COLOR 4. OMENTUM ADHERENT 5. FEW SMALL INFARCTS 6. PERISPLENITIS	INFARCTION PERISPLENITIS ATROPHY	AUTOPSY FINDINGS—PNEUMONIA
506	TORSION OF THE SPLENIC PEDICLE & GASTRO-LIENAL LIGAMENT WITH CONSTRICTING POLYTHENE BAND (540°)	27	1. MARKED DECREASE IN SIZE 2. SOFT & SPONGY 3. REDDISH-BROWN IN COLOR 4. OMENTUM ADHERENT 5. PERISPLENITIS 6. NUMEROUS SMALL INFARCTS	INFARCTION PERISPLENITIS ATROPHY	AUTOPSY FINDINGS—PNEUMONIA
507	TORSION OF THE SPLENIC PEDICLE & GASTRO-LIENAL LIGAMENT WITH CONSTRICTING POLYTHENE BAND (360°)	37	1. MARKED INCREASE IN SIZE 2. FIRM 3. SLATE-BLUE IN COLOR 4. PERISPLENITIS 5. FEW SMALL INFARCTS	CONGESTION PERISPLENITIS	ALIVE

In the short time since these studies were initiated, no cysts have been formed. Although infarcts are readily produced, they are small and characteristically fibrous in nature. Large hemorrhagic areas with subsequent liquefaction of the involved tissue have not been observed in these animals. Atrophy of the spleen has been a consistent finding in those animals which have died. From the observations made to date, it appears unlikely that vascular occlusion alone will progress to cyst formation in the spleen of dogs. This is a continuing experiment, and further findings will form the basis for a more complete report at a later date.

SUMMARY

1. The rarity of non-parasitic cysts of the spleen is emphasized by the report of recent cases. The total number found in the literature is 183, excluding the one herein reported.

2. A case of calcified cyst of the spleen is presented, bringing the total number of such cases to 31.

3. Splenic cysts have been classified as dermoid, parasitic, and non-parasitic.

4. The etiology of non-parasitic cysts of the spleen is not known.

5. Except for neoplastic types, the non-parasitic splenic cysts are thought to occur as a result of trauma, inflammation, torsion of the splenic pedicle, thrombosis of the splenic vessels, or as a result of the development of epithelial rests formed during the fetal period.

6. Splenic cysts must be considered in the differential diagnosis of any mass appearing in the left upper abdomen with or without associated pain or digestive disturbances. Calcification of such cysts is a rare occurrence.

7. The preliminary results of an experimental study following occlusion of the blood supply of the spleen in dogs is reported.

8. No evidence of changes suggesting cyst formation has been found in dogs examined up to ten weeks postoperatively. Infarction and atrophy are the characteristic pathologic findings. Continued observations of animals with total occlusion of the splenic blood supply will be made before a final report is presented.

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A list of references containing the reports of non-parasitic splenic cysts appearing since the end of 1944 may be obtained from the author.

SPLENIC ARTERY LIGATION IN PALLIATION OF ASCITES*

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NOT INFREQUENTLY the internist calls upon the surgeon for help in a case of advanced cirrhosis with uncontrolled ascites. Sometimes the patient presents a picture of extremely poor operative risk so that an extensive operation seems impracticable. In this situation the surgeon is interested necessarily in the less extensive palliative procedures, particularly if one can be found which will restore the patient fairly promptly to a state permitting more ambitious therapy. For the purposes of the discussion attention is directed to that group of cases of Laennec's cirrhosis in which ascites rather than hematemesis is the prominent feature.

Ascites is ordinarily considered to be the characteristic clinical feature of portal cirrhosis. It is found in 50 to 80 per cent of cases of cirrhosis (Bockus,[3] 1946), and perhaps in nearly 100 per cent of those patients who escape fatal hematemesis sufficiently long for ascites to develop. Ascites is the accompaniment and apparently the result of liver failure. Two-thirds or more of patients with cirrhosis do not suffer serious hematemesis, and most of these patients will die eventually of deranged liver function aggravated by uncontrolled ascites. During the final stages the situation known as "wasting ascites" often completes a vicious circle. With the deterioration of liver function there is a progressive hypo-albuminemia. When the falling plasma albumin approaches 3 Gm. per 100 cc. the albumin containing ascitic transudate appears (Blakemore,[1] 1948). In about half of the cases, even the most modern medical management fails to repair liver function sufficiently to restore the plasma albumin above this ascitic level (Patek, *et al.*,[6] 1948). If diuretics are ineffective, as they often are, ascites continues and increases so that paracentesis becomes necessary, and with each "tap" albumin is lost from the body to aggravate the already existing hypo-albuminemia. The patient with active liver disease, hypo-albuminemia, and ascites requiring repeated paracentesis is soon in desperate straits.

In the wards of a state teaching institution a considerable proportion of patients with cirrhosis have economic and social backgrounds such as to favor the development of "wasting ascites." The modern diet for cirrhosis, with meat three times daily, is an expensive diet. Alcoholism is a complicating factor in many cirrhotics. Often proper medical management proves impossible except during the hospital stay. The progressive nature of the disease becomes obvious on re-admissions, and before long the patient presents an

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insurmountable problem to the internist while the surgeon finds him to be a desperate operative risk.

In general the surgical procedures attempted in cirrhosis have been directed along one or another of the following lines:

1. Direct attacks are made against esophageal varices (ligation of tributaries, injection of veins, perivenous packing, or excision of the bleeding area by gastrectomy or esophago-gastrectomy). These procedures have been designed primarily to combat hematemesis rather than ascites.

2. Internal drainage of ascitic fluid is brought about (into the subcutaneous tissue, into the venous circulation, or into the excretory tract for the urine).

3. The abdominal venous return is increased by formation of added anastomoses between portal and systemic venous systems (omentopexy, visceropexies, and, more promising, operative creation of gross venous shunts).

4. Abdominal arterial inflow is reduced (splenectomy, splenic artery ligation).

The refinement of the technic of portacaval shunt during the past few years by Whipple[8] (1945), Blakemore and Lord[2] (1945), and others has resulted in a more hopeful approach to the problems of portal cirrhosis. Prior to this demonstration of the practicability of Eck-fistula type operations in selected cases, surgical therapy of liver cirrhosis had not had great success (Pattison,[7] 1949). Just how much it succeeded or failed is variously estimated, depending in part upon the personal experience of the surgeon expressing the opinion, and in part upon the extent of realization that many patients with cirrhosis have the good fortune that their disease undergoes spontaneous remission, and such patients may survive hematemesis and ascites for many years.

We have been particularly impressed with the possibility of spontaneous remission being mistaken for therapeutic triumph on reviewing the recent experience at our own institution in that combination of cirrhosis and splenomegaly called Banti's syndrome. For example, 18 cases were traced in which a typical Banti's syndrome had been treated by splenectomy alone. Of these eight had died, seven of them within the first year after splenectomy. But the other ten still survive, two to seven years after splenectomy, an average survival to date of 3.6 years since the operation and 4.9 years since the onset of the disease. The facts that 60 per cent of the 18 survived more than two years, and 44 per cent more than three years, suggest that splenectomy is fairly efficacious in Banti's syndrome. We would be tempted to emphasize this conclusion were it not for experience with the non-surgical management of the disease. Our hospital has been able to follow 14 recent patients with Banti's syndrome who had no surgery at all. As it happened everyone of these 14 cases suffered from hematemesis. Seven died within one year of the apparent onset of the disease, but the other seven, or 50 per cent, lived one to six years after the first hemorrhage, four of them surviving more than four

years; three of these latter are still alive. This is the record in a group of patients having no surgery. Though the percentage of survival after splenectomy is better, it does not appear nearly so convincing in view of these results in cases having no operation at all. Consequently, though we know of one of our own patients alive and symptom-free 15 years after the onset of ascites and hemorrhage, we do not know what value to place upon the surgery done in her case. Furthermore, we have become skeptical regarding the statement one often reads that among "untreated" cases 40 per cent are dead within one month of the first hemorrhage and 70 per cent within one year. No doubt the hematemesis of cirrhosis is a very dangerous development, but we believe that a fair proportion of patients survive it for several years.

The present report is restricted to cases of "wasting ascites." In the absence of data to the contrary it is our belief that spontaneous remission is very unlikely to occur once cirrhosis has reached this advanced stage. Furthermore, totally aside from the success with portacaval shunt in selected cases of hematemesis, nearly everyone will agree that when the advanced stage of "wasting ascites" is reached many patients will constitute exceedingly poor operative risks, hardly suitable for lengthy, formidable operative procedures.

Everson and Cole[4] in 1948 reviewed the few reports in the literature having to do with splenic artery ligation in portal hypertension and added three cases of their own in which the artery had been tied and an omentopexy performed. Results were encouraging in two of their three cases. Shortly thereafter we happened upon a very encouraging result in our first experience with splenic artery ligation in a patient in which omentopexy had given no relief. Consequently, in association with Dr. C. T. Stone, Professor of Medicine, we undertook to test the palliative value of the procedure in a series of consecutive cases of advanced ascites, intractable to medical management, and, in our opinion, too ill for a more extensive operation.

The normal plasma albumin of 4 Gm. per 100 cc. or more may fall in advanced cirrhosis to 2 Gm. per 100 cc. or less. Failure to increase after intensive medical treatment is of "grave import." Blakemore (1949) has reported that cases in which the value is 3 Gm. per 100 cc. or less are generally not good operative risks for a shunt procedure. He also stated that a bromsulfalein retention exceeding 35 per cent at 30 min. signifies poor operative risk.

Case 1.—O. R., white male, age 35 years, (No. 1206 OD) is one of two of our patients who had omentopexy in addition to splenic artery ligation. This man was a confirmed alcoholic with advanced cirrhosis. He had severe ascites requiring frequent "taps," but he had never had hematemesis. An omentopexy had given no relief. Five months later, after continued failure of medical treatment, the splenic artery was divided between ligatures (June 23, 1948). At this time the plasma albumin had fallen to 1.7 Gm. and the total protein to 3.6 Gm. per 100 cc. Cephalin flocculation was 2 plus but there was only 20 per cent BSP retention at 30 min. After splenic artery ligation an immediate remission in ascites occurred so that not one paracentesis was required

for 12 months. The patient was built up and he was able to return to fairly heavy work. However, 6 months after operation he was again drinking 2 one-fifth gallons of whiskey per day. After 12 months he suffered a relapse of ascites and when last heard from he had tissue edema and leg ulcers and required frequent "tapping." In view of the alcoholism we do not believe further surgical effort is indicated. However, splenic artery ligation had been followed by a rather amazing remission for one year.

Case 2.—A. R., a white male, age 6 years (No. 6863 E). This child had a congestive splenomegaly. There had been ascites for over 5 yrs., recently requiring many "taps." There had been no hematemesis. In spite of medical efforts his plasma albumin was 2.63 Gm. and total protein 4.5 Gm. per 100 cc. when he came to operation. Cephalin flocculation was 2 plus and BSP retention 20 per cent. A splenectomy was intended but the child tolerated anesthesia and laparotomy so poorly that only a splenic artery ligation with omentopexy was done. Within one month the plasma albumin was 3.0 and total protein 5.3 Gm. per 100 cc. There was an immediate amelioration of ascites and in the 17 months intervening paracentesis has never been needed. The spleen remains palpable but there has been no evidence of hypersplenism to date, though the child is being watched with this in mind.

Case 4.—M. P., white female, age 45 years (No. 250 F) was an alcoholic with cerebral disturbances, Korsakoff's psychosis, an unusual number of vascular spiders and a pronounced ascites requiring frequent "taps." There had been no hematemesis. At time of operation the plasma albumin was 2.25 and total protein 4.3 Gm. per 100 cc. There was 3 plus cephalin flocculation and BSP retention was 70 per cent at 30 min. She appeared so nearly moribund that we were hesitant to take her to the operating room, but on March 2, 1949, an immense splenic artery was divided between ligatures. After a few days of delirium there was marked improvement in every way except that the psychosis has persisted to the present. Within one month the plasma albumin had risen to 3.15 and the total protein to 7.85 Gm. per cent. In the 9 intervening months she has required no taps, but is in a mental institution and, because of the psychosis, we doubt that further surgery is warranted.

Cases 3, 5 and 6.—White males of 42, 49 and 59 years. (No. 6730 E, No. 4417 A, No. 6100), had severe ascites requiring many paracenteses. One carried a device in his pocket with which he tapped himself each week. He had had several hundred paracenteses. Two of these patients had had episodes of hematemesis 4 months and 10 years before. At time of operation the three averaged 2.5 Gm. per 100 cc. plasma albumin and 4.98 Gm. total protein. BSP retention ranged from 40 per cent to 90 per cent. The splenic arteries were ligated (December 1948, April and June 1949) and one month after operation the plasma albumin averaged 3.5 Gm. per 100 cc. All three patients showed improvement, though on a more moderate scale than the cases already reported. Patient number 3 died rather suddenly at home 3 months after operation; reportedly there was no vomiting of blood. Patients numbered 5 and 6 continued to show definite improvement for 6 months, with longer intervals between taps. At this time patient numbered 5 has begun to tap himself again and probably is experiencing a relapse.

We have ligated the splenic artery in a seventh case (8252 D), one of less advanced cirrhosis. In the 9 months since operation she has done well, but she had not required paracentesis before operation. However, she had had one episode of hematemesis 9 months before the ligation.

We have seen no evidence of damage having resulted from the splenic artery ligation in any of the seven patients. Ligation is said to cause a slow atrophy of the spleen. To date none of our cases has come to autopsy to test this. The only hospital death in connection with the study was that of still another patient who died of cholemia 26

days after we thought we had ligated the splenic artery. At autopsy it proved that only one division of a forked artery had been tied, so the case has not been included in the series. His spleen was not found atrophied. Since this autopsy we have tried to ligate well toward the midline, away from the splenic hilus.

Splenic artery ligation has two advantages over splenectomy. It is a less major procedure requiring less time, and it leaves intact most of the collateral venous channels about the splenic capsule. In performing splenectomy one sometimes destroys a fine omentopexy which nature has formed. The disadvantage of splenic artery ligation lies in the possibility that a renewed arterial supply to the spleen may develop with resumption of splenic functions or dysfunctions. To delay this as much as possible we have always divided the artery between ligatures instead of ligating it in continuity.

We have approached the splenic artery through a left oblique subcostal incision, dividing a part of the gastro-colic omentum. The natural hump the artery exhibits at the upper margin of the pancreas is apt to be increased when great enlargement of the spleen has pushed toward the right. We have even seen so tortuous an arterial elbow that in one instance we mistook the proximal for the distal limb and on dividing the vessel between ligatures were surprised to observe which end pulsated. It has been our practice to ligate each limb doubly, one of the ligatures transfixing the vessel, before the vessel is divided.

Although in some cases the artery is located and reached with ease, in other instances the vessel has been high and difficult of access. We recall a case of cardiac ascites where the spleen seemed greatly enlarged on abdominal examination. However, on opening the abdomen, the tumor proved to be a greatly enlarged left liver lobe. The spleen was too slightly enlarged for there to be any reason to ligate the splenic artery. Moreover, this small spleen was wedged upward behind the liver lobe into a position which would have made the artery almost impossible to reach from a subcostal approach. In two cases of cirrhosis it has been our impression that a spleen which was considerably enlarged had been displaced upward behind an enlarged left lobe of the liver in a way which made splenic artery ligation more difficult and hazardous. We have wondered if sometimes an enlargement of the left lobe of the liver occurring before splenic enlargement causes such displacement of the spleen. We have never used a thoracic approach or a direct approach to the coeliac axis through the epigastrium, as we have presumed that these routes would also be unsatisfactory if the liver was greatly enlarged.

To keep the operation as minor as possible, in the earlier cases we did not determine portal venous pressures, the diagnosis seeming obvious and being confirmed by liver biopsy in each instance. In three later cases, however, determinations were made and it was found that splenic artery ligation caused an immediate fall of 20 per cent or more in the portal pressure (440 mm. to 350 mm.; 345 mm. to 270 mm.; 470 mm. to 360 mm.). Linton, Hardy and Volwiler[5] (1948) recorded drops of 29 to 39 per cent after venous shunt in three patients.

In summary, division of the splenic artery between ligatures in six consecutive cases of advanced cirrhosis with "wasting ascites" and splenomegaly was tolerated by all six patients though they were poor operative risks from the standpoint of liver function. Three of the six patients showed an immediate and marked remission of ascites lasting 12 months in one case and still present at 10 and 17 months in the others. The remaining three patients showed less spectacular improvements. One died at home three months after operation, although we had thought he was doing fairly well. The other two showed moderate but definite clinical improvement, with a period of lessened ascites and enhanced response to protein feeding which has lasted about six months. It is our conclusion that splenic artery ligation holds considerable promise of palliation in many cases of "wasting ascites" with marked splenomegaly, cases of a group in which the splenic artery is said to carry as much as 40 per cent of abdominal arterial blood. Patients in deplorable state may improve sufficiently after the ligation that a more exten-

sive operation becomes feasible at a later date. However, we also wish to emphasize the caution necessary in evaluating any operative procedure in cirrhosis. Spontaneous remission, particularly in the less advanced stages of the disease, may account for much of the apparent benefit of therapeutic measures.

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DISCUSSION.—DR. WILLIAM C. CANTEY, Columbia, S. C.: My associate, Dr. George McCutchen, asked me to report a case of his. During the time he was in the Army he operated upon a 25-year-old white soldier with a calcified splenic cyst. The unusual feature was that this boy, even though he lived on a ranch, had no history of trauma, and his only complaint was low back pain. (Slides)

In this slide you will note in the upper left quadrant this calcified tumor mass. The diagnosis was made entirely by roentgen ray; all other laboratory examinations were negative. Here you see the tumor mass to be the cyst in a normal sized spleen. The cyst was about the size of an orange. It contained greenish viscid material without evidence of an endothelial lining. It was assumed to be the non-parasitic pseudo-type of cyst from a resolved hematoma, in spite of the absence of history of trauma. This was based on the fact that there was no serous lining, it was unilocular, singular, and without evidences of Echinococci.

DR. JAMES D. RIVES, New Orleans: I would like to report a single case that has some features similar to that of Doctor Martin. A middle-aged Negro had for eight months suffered from recurrent attacks of left upper abdominal pain associated with nausea and vomiting and development of a progressive anemia. During this period he noticed marked swelling of the abdomen which proved to be due to a tremendous tumor occupying the entire left upper quadrant. The mass was nodular and did not have the typical notching of the spleen. We considered the possibility of a cyst of the spleen but made no definite diagnosis.

At exploration, a huge splenic mass was found and removed without difficulty, since no adhesions were present. The mass measured 22 by 12 by 11 cm. and weighed 2115 Gm. On section it showed, at its upper pole, a small flattened mass that appeared to be compressed splenic tissue. The greater part of the mass was made up of what appeared to be a huge laminated clot surrounded by a dense fibrous capsule. Most of this clot was so old that it was yellowish in color. On histologic section this was determined to

be an organized clot. The splenic tissue showed only lymphatic and reticulo-endothelial hyperplasia with mild fibrosis and no malarial pigment. The capsule was composed of dense hyalinized material, in places calcified. This calcification had not been recognized on the roentgen ray films although irregular shadows were seen. At the junction of the splenic tissue with the hematoma was found evidence of organization with phagocytized blood pigment and some large endothelial-lined spaces filled with fluid and clotted blood. The pattern of these vascular spaces suggested cavernous hemangioma. The anatomic evidence suggests that this was a cavernous hemangioma of the spleen with massive hemorrhage, possibly related to unrecognized trauma.

BOOK REVIEWS

ANUS, RECTUM, SIGMOID COLON, Diagnosis and Treatment, by Harry E. Bacon, M.D., 1125 pages, Philadelphia, J. B. Lippincott Co., 1949. $30.00.

This is the third edition of a well-established text in proctology. The new edition represents a complete revision of the content with new material being added on such subjects as pre- and postoperative care, and the use of chemotherapeutic and antibiotic agents. All aspects of diagnosis and treatment are well covered. A very extensive bibliography, revised up to 1948, is provided at the end of each chapter. The author has carefully included all available and recognized opinions along with his own in presentation and discussion of controversial points. No effort has been spared to make this a complete and practical text and it should be a valuable addition to the library of the student and the general surgeon as well as the proctologist.

WILLIAM H. AMSPACHER, M.D.

REGIONAL ILEITIS, by Burrill B. Crohn, M.D., consulting gastro-enterologist, Mount Sinai Hospital, New York, 8°, cloth, 229 pp., with 74 illustrations. New York, Grune and Stratton, 1949. $5.50.

This volume is a compilation of the author's experience in the diagnosis and treatment of regional ileitis spanning an 18 year period, supplemented by a review of the literature. The book is well written and thorough; the many facets of this controversial subject are clearly presented and well documented. The illustrations are profuse, and of good quality. The type is easily readable and the paper is excellent.

Those interested in intestinal granulomata of the regional nonspecific type will find this work interesting and informative reading.

B. W. HAYNES, JR., M.D.

BALLOON TAMPONAGE FOR THE CONTROL OF HEMORRHAGE FROM ESOPHAGEAL VARICES*

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THE ADVENT OF THE BLOOD BANK, making large quantities of blood quickly available, has saved lives from ruptured esophageal varices. But, as has turned out to be the case with bleeding peptic ulcers, many patients will die if dependence is placed upon transfusions alone. In cases of peptic ulcer with persistent bleeding, operation has already proved its worth by reducing mortality in our hospital experience from 60 per cent to 5 per cent. So, in cases of bleeding from esophageal varices, if more lives are to be saved, a sure method of stopping hemorrhage at the bleeding site must be devised.

The concept of stopping hemorrhage at the site of a ruptured esophageal varix by tamponage is not a new one.[1-3] Our interest in the subject of balloon tamponage of the esophagus arose some ten years ago when we first began taking portal pressure readings in cases of portal hypertension. These pressure readings gave us the clue to the magnitude of pressure that would be necessary to collapse veins in the coronary-esophageal collateral circuit. By experiment it was determined that pressures of this magnitude (20 to 30 mm. of mercury) could be tolerated by the esophagus for considerable periods of time.

It is a fact, that the majority of cases, (75 per cent in our series), with bleeding esophageal varices have livers damaged by cirrhosis. It is equally well known that badly damaged livers tolerate anoxia from hemorrhage and shock poorly. Time after time patients may be brought out of shock by transfusions, only to be lost, days later, because of liver failure. It was our hope that if an efficient method of balloon tamponage could be made available for quick use in such cases, it would mean that the total quantity of blood lost might be greatly reduced. This would lessen the likelihood of immediate death from shock or delayed death from liver failure.

Knowing the relatively low magnitude of pressure necessary to collapse esophageal varices, it was hoped that traction upon a nasogastric tube bearing an inflated balloon in the stomach would be the simplest solution to the problem of hemorrhage. It is a fact that if sufficient traction is applied to a nasogastric tube, bearing an inflated balloon in the stomach, hemorrhage will cease. The balloon makes contact with and compresses the coronary veins at their junction with the esophageal veins and thus prevents the flow of portal blood through this collateral circuit.

* Read before the Southern Surgical Association, Hot Springs, Virginia, December 7, 1949.

The above described mechanism prevails irrespective of the contour of the balloons employed. When, for example, the balloons upon inflation are spherical or globular in shape, traction upon the nasogastric tube causes the upper portion of the balloon to ascend within the esophagus to some extent. This affords compression of the veins at the coronary-esophageal junction. If a sausage shaped balloon be employed, though a greater part of it be placed in the esophagus to start with, upon inflation its lower portion expands rapidly, globular fashion, into the stomach. Providing that the nasogastric tube is taped securely to the nose to afford counter traction to the downward thrust of the balloon again, satisfactory compression of the veins at the coronary-esophageal junction will be attained and hemorrhage will cease.

This method of employing traction upon a nasogastric tube bearing a balloon or balloons for the arrest of hemorrhage from esophageal varices has been used by many and described by some.[1-3]

Constant tension, however, upon a nasogastric tube with an inflated balloon jammed into the lower end of the esophagus exerts pressure upon the entire naso-esophageal tract and an upward pull upon the stomach. This serves to initiate reflexes which result in contractions of the stomach and esophagus. As these contractions become exaggerated, retching with convulsive attempts at regurgitation supervene. Thus is promoted a condition which gets beyond the human power of wilful control. Granted that the balloon may be inflated to a size that would resist regurgitation of the tube, nevertheless, continuous retching creates an impossible situation and, besides, causes a sharp rise in portal blood pressure.

To abolish regurgitation reflexes and effect tolerance to traction upon a nasogastric tube requires deep sedation in the average case and even anesthesia in some. Whereas these are undesirable features, and particularly so when dealing with cases of cirrhosis of the liver, nevertheless they do not cancel out the usefulness of a device which has proved to be life saving.

The above observations pointed out to us the need of an esophageal balloon so designed that once placed correctly in the esophagus and inflated, it will not mushroom into the stomach and thus create a drag upon the nasogastric tube.

It must be remembered that an esophageal balloon, to be effective in the arrest of hemorrhage from esophageal varices, must exert pressure upon veins from the coronary-esophageal junction upward. Thus the lower end of the balloon must project slightly into the stomach. To prevent over-expansion during inflation of that lowest portion of the sausage-shaped esophageal balloon which projects, unsupported, into the stomach, the idea occurred to one of us (R. W. S.) of reinforcing the lower one-third of the balloon with a double thickness of rubber. This reinforced, self-retaining, esophageal balloon was first employed by us in September, 1946. The case was that of a 15-

year-old girl suffering from a severe attack of hematemesis due to portal hypertension, secondary to extrahepatic portal block. At first the bleeding was stopped in the usual manner, employing the traction principle of balloon tamponage as follows: A triple lumened nasogastric tube bearing two balloons was passed. The lowermost spherical-shaped balloon was inflated in the stomach, following which the nasogastric tube was withdrawn just snug and taped securely to the nose. Finally, the upper esophageal balloon was inflated. During inflation of this balloon, the nasogastric tube became taut and began to pull upon the nose. The pressure in the balloon rose during inflation to 30 mm. of mercury but only after 200 cc. of air had been introduced, at which point bleeding ceased. Shortly afterward, in spite of sedation, the child began to retch and finally regurgitated the tube with the inflated balloons intact.

Because of the recurrence of bleeding in this case, a second attempt was made. In this instance, a nasogastric tube bearing a special sausage-shaped esophageal balloon was passed. The balloon was identical in size and shape to the balloon previously used except for the important difference that the lower one-third was reinforced with a double thickness of rubber. Inflation of this balloon resulted in a startling difference: the mercury in the manometer began to rise immediately and, following the injection of only 50 cc. of air, bleeding from the esophageal varices ceased entirely. This small amount of air compared to the 200 cc. required in the unreinforced balloon to accomplish the same result.

The obvious reason for the difference in behavior between the unreinforced and the reinforced balloons during inflation is that the lower end of the unreinforced esophageal balloon expands, globular fashion, into the stomach and thus consumes great quantities of air; whereas, the double thickness of rubber at the lower end of the reinforced balloon resists overexpansion and forces the air to exert equal pressure upon the esophageal veins throughout the length of the balloon. Because of this special design, promoting equalization of pressure, there is no tendency for the reinforced esophageal balloon to mushroom into the stomach and cause the dreaded drag upon the nasogastric tube. The facts are that the balloon remained inflated with complete control of hemorrhage in this 15-year-old child for a period of 48 hours. Though only light sedation was employed, the patient made no serious effort to regurgitate the tube.

In Figure 1 is shown a satisfactorily designed tube for balloon tamponage of the esophagus.* Note the generous size of the main, central lumen of the tube. This is essential to permit aspiration of old blood from the stomach and for feeding in certain cases. The tubes to the balloons are relatively small and are incorporated in the outer wall of the large tube. The distal balloon, when inflated in the stomach has a primary purpose as a marker for quick and proper positioning of the upper balloon in the esophagus. Although

* Made according to our design by the Davol Rubber Company, Providence, R. I.

there is a radiopaque marker incorporated in the wall of the tube between the balloons, roentgenograms are not necessary in the average case. The most important feature of the whole assembly which shows up least in the photograph is the reinforced area of the esophageal balloon: note the shading of double thickness rubber in the distal third of the balloon.

The specially designed esophageal balloon has been employed by us for the control of bleeding from esophageal varices in 30 patients with outstanding success. There were no deaths from shock due to hemorrhage and, in our opinion, many pints of blood were saved. In addition to its efficiency in stopping hemorrhage, an asset of primary importance is the fact that the tube and balloon are well tolerated by the average patient and may be employed for long periods of time.

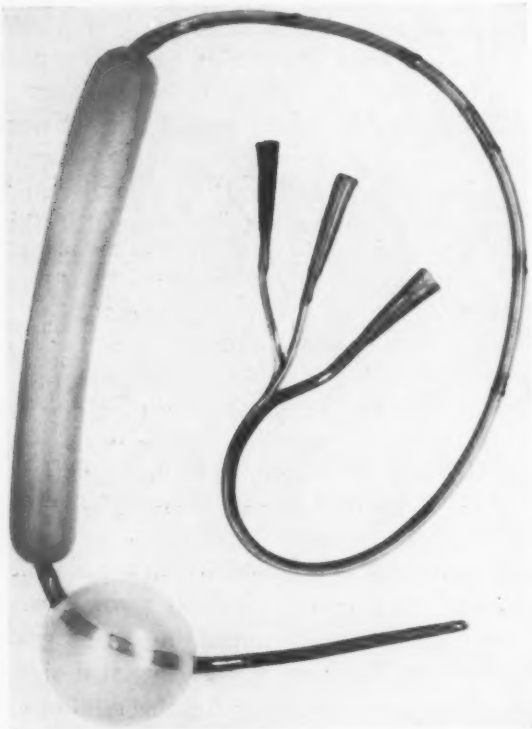

FIG. 1.—A photograph of a naso-gastric tube-balloon assembly for the emergency control of hemorrhage from esophageal varices. Note the generous size of the tube for gastric suction. Observe that the distal one-third of the sausage-shaped esophageal balloon is more shaded, indicating a greater thickness of rubber. A metal roentgen ray marker is incorporated in the wall of the tube between the balloons.

It is now well known that in cases of cirrhosis with severe liver damage bleeding from esophageal varices may be unduly prolonged because of an alteration in the clotting mechanism, due to hypoprothrombinemia. This was well illustrated in one of our recent cases in which the nasogastric tube was left in place for a period of seven weeks, during which period the patient was tube fed. This 56-year-old man with serious liver failure started to bleed from his esophageal varices the moment the pressure in the esophageal balloon was released. This performance continued for many weeks, during the most part of which he was semistuperous from cholemia. On admission he was deeply jaundiced, and had ascites and peripheral edema. He rapidly developed enlargement of both breasts, testicular atrophy and a falsetto voice; his cholesterol esters were but 12 per cent of the total. The bromsulfalein retention was 55 per cent one-half hour after injection and the serum albumin 2.3 Gm. per 100 cc. Amazingly enough, four and one-half months after

admission, the patient rather suddenly began to improve. At eight months following onset, he is back at his job as an editor.

It is a frequent experience that patients with severe cirrhosis bordering on cholemia, when suddenly complicated with hemorrhage from esophageal varices, will die promptly of total liver failure, transfusions notwithstanding. Never, in our experience, has a patient as ill as the one above cited survived. It is true that we also used transfusions and hykinone in abundance on this patient during the critical several weeks.

Notwithstanding, one could best judge the prevailing incapacity of his blood to clot simply by releasing pressure in the esophageal balloon and aspirating a sample of stomach contents. The patient proved to have small esophageal varices, scarcely demonstrable by roentgen ray. This is suggestive evidence that the blood clotting dyscrasia and not the degree of portal hypertension was largely responsible for the tendency to prolonged bleeding from the varices. It is our considered conviction that the control of blood loss with balloon tamponage was the most important factor in saving this man's life. Another feature of interest is the large amount of protein and carbohydrate feeding mixture this patient consumed daily via gavage feedings.

The Sengstaken, reinforced, esophageal balloon is assuming a role of increasing importance in preparing those cases of portal hypertension complicated by hemorrhage for the portacaval shunt operation. There are many patients with cirrhosis of the liver who, because primarily of a severe grade of portal hypertension, have one attack of hematemesis after another with grave regularity. Such patients are doomed to die and very soon, unless they obtain operative relief. In our series of 71 cases of cirrhosis in which a portacaval shunt has been established, there are 15 cases belonging to this desperate group. Surprising though it may seem, 13 of the 15 patients survived.

The nasogastric tube bearing the reinforced esophageal balloon did yeoman service in this group in affording control of hemorrhage during that treacherous period of transfusions to bring up the blood volume and red blood cell mass to normal before operation. The tube covered a longer period of forced nutrition in one case in whom transfusions could not be used preoperatively because of violent febrile reactions to as little as 50 cc. of blood. This patient, though she was jaundiced and had a badly functioning liver in some other respects, survived a side-to-side portal vein to venacava anastomosis, in spite of receiving several transfusions while under anesthesia. Her postoperative course was stormy, but she is alive and symptom-free. All roentgen ray evidence of esophageal varices are gone and she has been free of hemorrhages now for nearly two and one-half years since operation.

It is of interest that in the group of chronic, recurring bleeders, there are two cases of partial portal vein thrombosis. One patient with an old thrombus which had become covered with intima got an excellent result following an end-to-side anastomosis of the portal vein to the venacava. The patient is

active and has been free of hemorrhages now for more than one year since operation.

The second patient had a thrombus of about the same size, (40 per cent of the diameter), but of more recent origin. The intima had not covered the thrombus. A small hematemesis occurred immediately after an esophagram made on the sixteenth day following an end-to-side anastomosis of the portal vein to the venacava. Though the roentgenograms showed the varices to be smaller than before operation, we concluded that the anastomosis was either occluded or inadequate in size and that a splenorenal shunt was indicated. Accordingly, a nasogastric tube was passed and balloon tamponage established. Over a ten-day period, the patient was given a high protein-carbohydrate mixture by gavage. The blood volume and red blood cell mass were brought up to normal. At this point, the patient went through a splenorenal shunting operation which was followed by an uneventful recovery. Following this procedure, repeated roentgenograms of the esophagus failed to reveal any varices. The patient had had no further episodes of hemorrhage when last heard from.

Some idea of the drain incurred upon blood banks in trying to keep these chronic, recurring bleeders alive on transfusions alone may be illustrated by the following case of a 36-year-old white male with Laennec's cirrhosis who, during a year of treatment under the Patek regimen, had shown marked improvement of liver function. His jaundice, ascites, and leg edema had cleared but the hepatosplenomegaly had persisted. Likewise, roentgenograms of the esophagus following a barium swallow revealed large, extensive varices.

Six weeks prior to the patient's admission to the Presbyterian Hospital, two severe hematemeses occurred, four days apart. The estimated blood loss of 4500 cc. was replaced by transfusion. From the day of the patient's admission to the medical ward of the Presbyterian Hospital until the day of his transfer to Surgery, over an interval of 21 days, this patient had nine hematemeses. The estimated blood loss over this period totaled 14,700 cc. of blood. A total of 16,000 cc. (22 pints) of blood was given in replacement therapy. In spite of this, the patient was in severe shock at least once. On several occasions it was feared that the patient was going into coma because of a state of stupor.

On the night of transfer to the Surgical Service, the patient had a hematemesis of 2700 cc. Bleeding was promptly checked by a reinforced esophageal balloon. The patient was given 2500 cc. of blood during the night and a portacaval shunt, anastomosing the portal vein to the venacava, end-to-side, was performed the next day. The patient recovered from the operation and has had no further hemorrhages, now nearly a year since operation.

It may be that this patient's need of 22 pints of blood over a 21-day period could be supplied by an average community hospital. The facts are, however, that on the occasion of severe shock, this man consumed 12 pints (6000 cc.) of blood, over a 24-hour period. It is our opinion that such patients would

have a far better chance of coming through alive if the average hospital were equipped for balloon tamponage. Furthermore, estimating the over-all cost of blood at $30.00 a pint, this patient alone could have equipped 55 community hospitals for balloon tamponage.

For some time, in our papers on portacaval shunt,[4, 5] we have stressed the usefulness of this simple device.

Figure 2 is a photograph showing equipment with the naso-gastric tube in place.

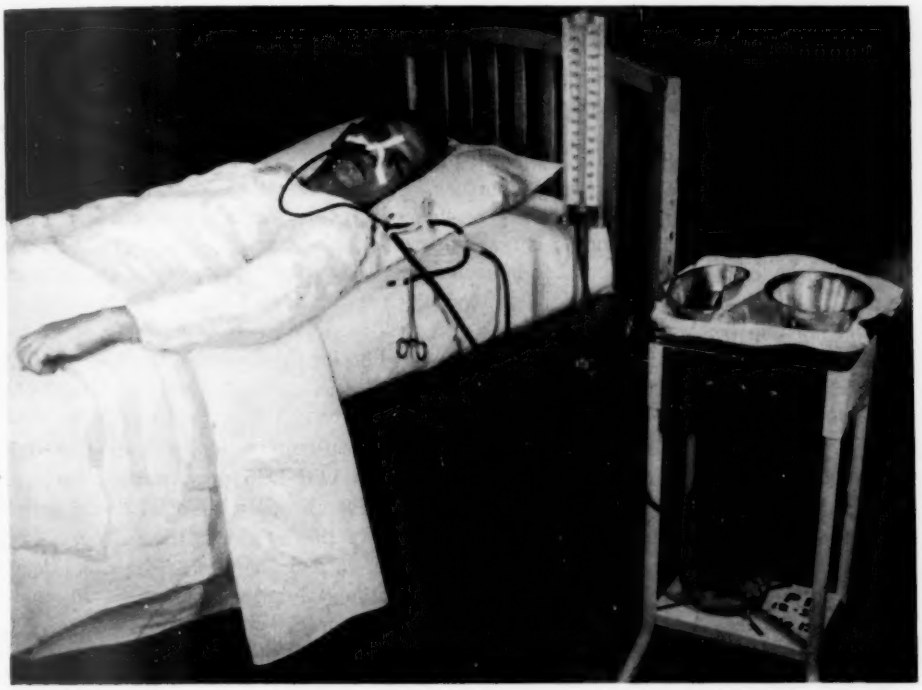

FIG. 2.—A photograph showing a patient having esophageal balloon tamponage.

INSTRUCTIONS FOR PASSING THE ESOPHAGEAL BALLOON FOR THE CONTROL OF BLEEDING FROM ESOPHAGEAL VARICES

Equipment Needed:

1. Esophageal varices tube with balloons attached.
2. Mercury manometer or Aneroid gauge of the Tycos sphygmomanometer to be connected with a "y" glass tube to upper sausage balloon.
3. Fifty cc. syringe.
4. Constant intestinal suction machine.
5. Lubricating jelly (not petroleum jelly).
6. Glass of water with straw.
7. One clamp for rubber tubing such as a Crile, Kelly, or Kocher hemostat.

Instructions for Passing the Tube:

A. Coat the lower part of the tube and the balloon with a thin coat of lubricating jelly.

B. After spraying the nostrils and the posterior pharynx with cocaine or butyn, pass the tube through the nostril until the tip is in the posterior pharynx or throat. Then, with swallows of water sipped through the straw in the glass of water, pass the tube to at least the 50 cm. mark. Next, inflate lower balloon with 150 to 200 cc. of air and withdraw tube slightly until resistance is encountered. Then inflate the upper sausage balloon to 20 mm. of mercury pressure and finally tape tube to nose securely.

C. Next, aspirate the stomach so that all of the blood is out of the stomach as well as air and swallowed water. During the aspiration, it is advisable to irrigate the tube frequently with at least 40 cc. of water to prevent the tube from clogging due to blood clotting.

D. Adjust pressure in upper balloon until bleeding ceases as determined by aspiration, usually 20 to 25 mm. of mercury as read on the manometer connected to one branch of the glass Y tube. When the balloon is in the proper position, the pressure will vary with cardiac and respiration pulsations and with contractions of the esophagus which may raise the pressure to 70 mm. of mercury. The pressure should not fall much below the above mentioned pressure. This pressure will require approximately 40–60 cc. of air. If more air than this amount is needed to give an adequate pressure (viz. 200 cc.), one may be fairly certain that the balloon is well out of the esophagus and into the stomach and hence down too far. After sufficient air is placed within the balloon, securely clamp the branch of the Y tube that was used to inflate the balloon so that it will not leak air. Check the pressure frequently to be sure that no leakage has occurred. A portable roentgenogram may be taken at this point to check the position of the tube. See the paragraph on construction of the tube.

E. Then connect the stomach aspiration tube to constant suction, irrigating the tube with 40 cc. of warm saline every half hour. This will help prevent the tube from being clogged with blood clot. The stomach must never be allowed to fill as the patient will then regurgitate the tube. Keeping the head of the bed elevated also helps keep the stomach empty. This also helps to decrease nausea and gagging. Adequate sedation is absolutely essential. We generally use sodium amytal intravenously and intramuscularly. This may be supplemented with Demarol if necessary. It is not necessary to keep the patient unconscious, but a slightly stuporous state is desirable at first. Regurgitation is due to two causes usually, the most important is lack of sedation, and the other is allowing the stomach to become filled. Bleeding should be stopped and the stomach can be kept free of blood once adequate pressure is maintained upon the esophageal wall. If the tube should be regurgitated, it should be re-passed immediately and without hesitation.

F. The tube with the balloon inflated should be kept at the minimal pressure required to control bleeding, approximately 25 mm. of mercury for at least 48 hours and then deflated for 12–24 hours to see if new bleeding occurs. If none occurs then the balloon may be slowly withdrawn with very little danger of starting new bleeding. During the time that the balloon is in place, the patient must be kept hydrated and can be given some nutrition by intravenous or clysis fluids. Feedings can be given through the stomach part of the tube, 100 to 150 cc. per hour, with the head of the bed elevated and the patient on his right side. If all goes well, the stomach may be aspirated just before feedings. Too thick feedings must be avoided as they will clog the tube and remain in the stomach an undue length of time. It must be remembered that placing too much feeding within the stomach will increase the dangers of vomiting the tube, and therefore extreme caution must be used for there is great variability in the tolerance of patients.

In cases requiring prolonged tamponage, tube feedings are more important. The following is a good formula for cirrhosis cases:

		Proteins Gm.	Carbohydrates Gm.	Fats Gm.
Skimmed milk	= 1500 cc.	75	60	0
Eggs	= 3	19	..	17
Glucose "Dyno"	= 120 Gm.	..	120	..
Protein hydrolysate "Protinol"	= 100 Gm.	61.5	30	..
Ground liver	= 200 Gm.	47	..	33
		202	210	50

Add water up to 2400 cc.
Total calories = 2098 for 24 hour intake.

Glucose and protein hydrolysate proportions may be varied to alter Protein and Carbohydrate ratio.

G. It is important to emphasize that the patient is to swallow nothing, not even saliva, once the tube is in place. In cases having excessive mucus accumulation the balloon may be deflated for a few minutes several times a day.

H. After the tube has been withdrawn, the patient may be started on clear fluids and slowly advanced to a soft diet.

I. If, after the esophageal balloon is inflated to as much as 30 to 35 mm. of mercury, repeated aspirations from the stomach reveal bright red blood, it usually means the source of bleeding is from a coronary vein on the stomach wall: a rare occurrence in our experience. In this event, the patient is given additional sedative at once, the nasogastric tube is snubbed up firmly and taped securely to the nose. Finally, the stomach balloon is inflated with more air gradually, to avoid retching. It may require a total of 300 to 400 cc. of air to arrest bleeding.

SUMMARY

A nasogastric tube with a specially designed esophageal balloon is presented for the emergency control of hemorrhage from bleeding esophageal varices. The device is well tolerated by the average patient under mild sedation. Cases are cited to illustrate its usefulness.

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BILIARY TRACT HEMORRHAGE: A SOURCE OF MASSIVE GASTRO-INTESTINAL BLEEDING*

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THE UNDETERMINED SITE of massive gastro-intestinal hemorrhage is a constant challenge to the clinician and consultant. In reviewing the origin of hematemesis and melena, the conclusions of several authors[1-3, 5, 8, 27] indicate that 2 to 5 per cent of the cases are tabulated "gastro-intestinal hemorrhage —source undetermined." The biliary tract is rarely considered in such a differential diagnosis of massive hemorrhage. The purpose of this report is to stimulate interest in the liver and biliary tract as a source of bleeding in patients having gastro-intestinal tract hemorrhage which eludes diagnosis by the usual studies.

CASE REPORT

R. P., a 35-year-old Jewish male, was first seen May 22, 1949, with the complaint of epigastric pain and faintness. His past history revealed that in 1931 the right testicle was removed for an embryonal teratoma. This was followed by deep roentgen ray therapy which was given for palpable metastasis. Sufficient roentgen ray was given to produce irradiation dermatitis. In 1934 the deep roentgen ray treatment was repeated for the complaint of recurrent abdominal pain. An appendectomy was performed in 1938 and a Torek procedure on the left testicle in 1939. In 1945, while in Portugal, the patient developed a syndrome of diarrhea, during which ulcerations of the rectum were found. Repeated examinations of the stools failed to demonstrate any pathogens. Shortly after his return to the United States he developed abdominal pain with a definite food relationship which suggested peptic ulcer to his physician. In October, 1947, he was admitted to the hospital for a recurrence of the pain. Marked anemia was present, but roentgenograms showed no lesion in the gastro-intestinal tract. Transfusions failed to produce a satisfactory response and he continued to pass tarry stools. A sub-total gastrectomy was performed as an emergency procedure, although a definite ulcer could not be demonstrated in either the stomach or the duodenum at the time. The pathologist was unable to demonstrate any ulcer in the resected surgical specimen. Six months after the operation he developed an attack of epigastric pain in the left upper quadrant associated with mild shock and was first seen by one of us (M. M.). He was hospitalized, and study demonstrated the mild transient acute pancreatitis evidenced by elevation of the serum amylase, hyperglycemia and glycosuria. He responded well to symptomatic measures and following his recovery a complete gastro-intestinal roentgen ray study and cholecystogram were done. No evidence of pathologic changes in the stomach, small or large bowel, or gallbladder was obtained. At the present admission he again complained of pain in the epigastrium and faintness, and passed a black tarry stool. This pain was not related to the ingestion of food in any way, and was colicky in nature. There had been no vomiting of blood at any time and no associated nausea. Roentgenograms again failed to show any evidence of gastric, marginal, or jejunal ulcer and the barium enema study was again reported negative.

* Read before the Southern Surgical Association, Hot Springs, Virginia, December 7, 1949.

Gastroscopy showed no intrinsic lesion within the stomach or at the site of the gastro-jejunal anastomosis, but it was noted that there was brownish material welling up in the proximal end of the gastro-jejunostomy loop.

On physical examination the patient was markedly emaciated, his weight being 99 pounds as compared to 130 pounds before his partial gastrectomy. The pertinent findings were limited to malnutrition, anemia and to the abdomen. There was evidence of irradiation, and telangectasia was noted in the skin of the anterior abdominal wall. Moderate epigastric tenderness was noted. The laboratory studies reported a hemoglobin of 74 per cent, R.B.C. 3.4 million. All of the blood chemistry was within normal limits with the van den Bergh, 0.2; the B.S.P. test was negative, cephalin flocculation test was negative. All stools were positive for occult blood. He was given 5 transfusions and was discharged from the hospital with the recommendations that he should submit to laparotomy. A month later he began to bleed again, passing large black tarry stools, and developed weakness and dyspnea with mild exertion. He was again admitted to the hospital. Laboratory and roentgen ray studies were repeated without revealing further information.

Laparotomy was performed on June 22, 1949. On opening the abdominal cavity the viscera were thoroughly explored. It was noted that there was a small tumor in the duodenal stump and after opening the duodenum to remove this polyp it was noted that it was perfectly clean and healthy. The gallbladder was then compressed and, to our amazement, bloody bile exuded through the papilla of Vater. The gallbladder and then the common duct were aspirated and bloody material was found in both. The common duct was opened and a perfect blood clot cast of the common duct and the radicals of the common hepatic duct was found and removed. No stones, ulcer or tumor were found either in the biliary tract or in the gallbladder. Palpation and probing of the hepatic radicals failed to disclose the presence of tumor or stone. Bloody bile came down both the hepatic radicals into the common hepatic duct and it is therefore assumed that the hemorrhage was hepatic in origin. The gallbladder was removed and a T-tube implanted in the common duct. The convalescence was entirely uneventful. During his recovery a specimen of bile was collected and a cytologic study done. The pathologist was unable to find any cells suggestive of tumor. Two cholangiograms done before removal of the T-tube showed no abnormality of the biliary tract. The patient was discharged from the hospital on his sixteenth postoperative day in good condition. Since that time he has had lobar pneumonia, following which he passed tarry stools on 2 days. He has gained 8 pounds of the weight lost. Skin tests and complement fixation tests for schistosomiasis are negative. Repeated studies of his blood, coagulation time, prothrombin time, marrow, etc., have all been normal. There has been no recurrence of bleeding since August, 1949.

DISCUSSION

The above record illustrates the problems of accurate diagnosis and rational treatment for the patient having repeated massive gastro-intestinal hemorrhage. In this case intrahepatic biliary tract bleeding is the origin of the repeated hemorrhages.

Biliary tract hemorrhage was first reported by Nauyn in 1892 and by Schmidt the following year.[19] We were able to find less than 100 subsequent case reports on the subject. Only reports of an acholemic patient with fatal or near fatal hemorrhage arising from the biliary tract have been considered.

Nauyn (1892) Budinger (1925) and Lichtman (1936),[19] have classified hemorrhage due to diseases of the liver and biliary tract. Lichtman's classification is anatomical, simple and clinically sound. It is as follows:

TABLE I.—*Classification of Hemorrhage Related to Diseases of the Liver and Biliary System (Lichtman 1936).*

- A. Acholemic
  - 1. Portal in origin
    - a. Varices
    - b. Thrombosis of portal vein
  - 2. Hepatic in origin
    - a. Trauma
    - b. Yellow atrophy
  - 3. Biliary tract in origin
    - a. Vascular
      - 1. Ruptured aneurysm
      - 2. Erosion of blood vessel
      - 3. Perforation of gallbladder
    - b. Hemorrhagic cholecystitis
    - c. Neoplasm with ulceration
- B. Cholemic dyscrasia

We have further subdivided biliary tract hemorrhage into intra- and extrahepatic sources because of the difference in clinical manifestations.

TABLE II.—*Sources of Biliary Tract Hemorrhage: Reported.*

- A. Intrahepatic
  - 1. Post traumatic
  - 2. Subacute yellow atrophy
  - 3. Hemangioma
  - 4. Central apoplexy
    - a. Aneurysm hepatic artery
- B. Extrahepatic
  - 1. Bile ducts
    - a. Calculus
    - b. Ulcer—benign with erosion hepatic artery, portal vein, etc.
    - c. Aneurysm
      - 1. Cystic artery
      - 2. Hepatic artery
    - d. Cavernomatous transformation of the portal vein
    - e. Carcinoma ampulla of Vater
  - 2. Gallbladder
    - a. Calculus—erosion cystic artery, etc.
    - b. Ulcer
    - c. Hemorrhagic cholecystitis (hemocholecyst)
    - d. Cancer of gallbladder
    - e. Cholecystitis glandularis proliferans

Intrahepatic hemorrhage into the bile ducts may be due to trauma,[13, 25] subacute yellow atrophy,[19] hemangioma,[5] central apoplexy or rupture of an hepatic artery aneurysm.[28] It should be emphasized that in the reports of post-traumatic hemorrhage, the gastro-intestinal bleeding occurred five to seven weeks after the injury. In one instance, studies for peptic ulcer were made before laparotomy proved the diagnosis of hepato-biliary tract hemorrhage.[13] Therefore, history of injury to the abdomen or lower right chest may lead one to suspect the liver if subsequent hemorrhage occurs. The intrahepatic sources are quite rare as compared to those of the extrahepatic biliary tract. This is a fortunate circumstance since the extrahepatic group is surgically accessible for correction or removal.

The most common cause of extrahepatic biliary tract hemorrhage is the gallstone.[14, 15, 21, 22, 24, 18] The most frequent site of the hemorrhage is in the gallbladder. Other causes of cholecystic bleeding are hemorrhagic cholecystitis, hemocholecyst, benign ulcer, trauma, cancer and finally the rare polypoid condition known as cholecystitis glandularis proliferans.[10, 13, 15-17, 19, 21, 22, 29]

Hemorrhage is an important consideration in cases of cholelithiasis. White[29] reported six cases of massive hemorrhage, one of which resulted from a stone left in the cystic duct stump after cholecystectomy. A considerable number of patients with so-called quiet stones have anemia associated with the presence of occult blood in the stool.[15] In the absence of other sources these findings may suggest previously unsuspected gallbladder disease. We have noted the presence of old blood clots in gallbladders removed for calculus. Lichtman[19] believes that there is evidence of gross hemorrhage in 1 to 5 per cent of all patients with gallbladder pathology. There are several reports in the literature of massive hemorrhage associated with cholecystitis and hemocholecyst. There are only two reports[13, 17] of hemorrhage from the gallbladder following external trauma. These were due to laceration of the cystic artery which produced shock, hematemesis and melena. Although rare, Hudson and Johnson,[15] Fiessinger, *et al.*,[10] Sainburg and Garlock[26] and Lichtman[19] report occasional massive gastro-intestinal bleeding in patients with primary cancer of the gallbladder; *i.e.*, carcinoma and hemangiosarcoma.

Study of these reports of patients presenting massive hemorrhage which originated in the gallbladder leads to the following conclusions. Nearly all patients with stones gave a history of previous episodes suggesting colic before the hemorrhage. Those having tumor or hemorrhagic cholecystitis presented a right upper quadrant mass in the region of the gallbladder associated with tenderness, fever and hemorrhage. In the cases of traumatic hemorrhage the history of injury was always given even though the gallbladder was not suspected as the source until operation. We believe, therefore, that we should be able to predict the origin of hemorrhage in this group of patients by past history, physical findings and exclusion of the more common causes of massive hemorrhage.

The diagnosis of primary extrahepatic bile duct hemorrhage is more difficult. Massive bleeding from the ducts has been reported due to stone, benign ulcer,[19] rupture of hepatic artery aneurysm,[11, 19] erosion of the cystic,[29] hepatic or portal vessels, and to cavernomatous transformation of the portal vein with rupture into the common bile duct.[19] It is of considerable interest that several authors make no mention of hemorrhage being associated with benign papilloma[4, 6, 9, 20] of the common duct, papilla of Vater or the gallbladder. One may conclude that it must rarely occur with these benign tumors. However, malignant ulcerations[5, 7-9, 20, 23] of the ampulla of Vater are frequently associated with gross and massive hemorrhage. Cooper[7] states that occult or frank hemorrhage occurs in all patients having ampullary car-

cinoma. Eusterman[8] reported that in a group of patients undergoing surgery for undiagnosed gastro-intestinal bleeding, carcinoma of the ampulla of Vater was a frequent unexpected finding. This finding emphasizes the value of duodenal drainage for the study of its contents in patients having negative gastro-intestinal roentgen ray studies. Cytological study of these contents should be a further aid in establishing a preoperative diagnosis of ampullary carcinoma at an earlier date.

SUMMARY

1. A case report of intrahepatic biliary tract hemorrhage is presented.

2. The problem of biliary tract hemorrhage as a source of massive gastro-intestinal bleeding is discussed.

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DISCUSSION.—DR. JOSEPH E. J. KING, New York: I have enjoyed Doctor Blakemore's paper very much and am pleased to see his most intriguing apparatus for control of this terrible condition. You need see only one of these patients die before your eyes to realize your helplessness in such a situation. It's like watching a man drown without being able to do anything about it.

About ten years ago I operated upon a man who was chief officer on a merchant marine ship for an encapsulated brain abscess of the left temporal lobe. It was one of the easiest to deal with and operate upon that I have ever seen, and we expected a good result in a fairly short time. He was about 42 years old and a known syphilitic. About the fifth postoperative day a massive hemorrhage of bright blood took place and his condition became very poor. We felt sure the hemorrhage was from varices of the esophagus but we did not know how to control it. I knew that electrocoagulation had been done on a few occasions successfully, but we did not want to attempt it in this case because of possible rupture of the brain and provoking hemorrhage through struggling. So we did nothing for the time being but observe him and wait. We then gave him a small transfusion of blood and he improved. Just about the time he seemed to be doing fairly well he had another severe hemorrhage. This recurred five times. Each time we gave him a little blood and his condition became somewhat better, he would have another hemorrhage. After the fifth one, he died on about the fifteenth postoperative day.

Autopsy revealed a large opening in a varix, so large that it admitted the blunt end of a mortician's needle. The spleen was greatly enlarged to about three times its normal size. The liver, instead of having the appearance of a normal liver, was discoid in shape, about 12 inches in diameter, and was somewhat the shape of a loaf of black Polish bread, narrower at the edge than in the middle. I would say it was not more than 3.5 inches in thickness at its central portion. Of course, the hemorrhage could have been controlled readily had one been able to put his finger on the small hole and hold it, but this could not be done. I thought of all sorts of things to do, like tamponading the esophagus with a gauze packing, or making some sort of apparatus shaped like the old-fashioned cattail that grows in a swamp, and pushing this down into the esophagus and holding it there. However, none of these things were done.

Just a few weeks ago, shortly after I received the program for this meeting, I glanced through it and saw the title of Doctor Blakemore's paper. I had not the slightest idea what it was about so far as the rubber bag was concerned. A few evenings later I was called away from a surgical meeting by one of my colleagues. He told me about a patient with an enormous plum-colored hemangioma occupying about half of his face, who had sustained a hemorrhage of bright blood from his throat. I was told he had had a hemorrhage from a varix. Having remembered the one word "balloon" from the

title of Doctor Blakemore's paper, a few ideas came into my head. I told my colleague to get a few things ready immediately, particularly a Levin tube and two condoms, so that we could pass the Levin tube through the man's nose, pull it out through his mouth, place one condom inside the other for reinforcement with 3 or 4 cc. of water inside the condom, and fix the open end water- and air-tight about the Levin tube; then let the man swallow the rubber bag down to the position of the varix. It was believed that the rubber bags could be swallowed better with a small amount of water in the distal end than empty, and that by trial and error we could blow up the rubber bags, control the hemorrhage, and fix the tube to the nose to prevent displacement. I thought it would readily control the hemorrhage, and from what I have heard from Doctor Blakemore I know now that it would. We also anticipated as soon as the man's condition permitted, doing a quick gastrostomy under local anesthesia for feeding him, and leaving the tamponade in position as long as was necessary.

Fortunately, the man did not have an esophageal varix. He had a hemorrhage from a hemangioma inside his nose, and he spit out the blood. So I did not get to use my trick, but I have a notion that it might work out all right out in the country where I live, and where we do not have the advantage of this ingenious device of Doctor Blakemore's.

Now I keep such things handy, for when you need these things you need them bad. I might add that a long Penrose drain sealed at one end would also answer the purpose.

Dr. Allen O. Whipple, New York: I have no such interesting case report as Doctor King has given you; he always gives interesting reports. I do wish to take this opportunity to express my true appreciation and admiration for the work Doctor Blakemore has done in this field which, when it was started a number of years ago, appeared to be rather hopeless. It was started because we had so many patients coming back with recurrent hemetemesis following splenectomy for Banti's syndrome. And it was because of Doctor Blakemore's interest in vascular surgery that attempts were begun to control this, and I have been interested since then in his work. Only one who has worked with Doctor Blakemore can have any appreciation of his perseverance, his "never say die" attitude. I shall never forget some of the cases with which I have helped him. I tried to persuade him to stop, but not at all—he went right along. It is this perseverance in a difficult field, to which he has contributed so soundly, that has been evidenced today, because patients coming for surgery for portal hypertension very often bleed right under your eyes, as in the case he reported, the day before he was to operate. It seems to me that this device of his, which is an improvement over previous attempts, is a real life-saving apparatus, and I think he deserves great credit for persevering as he always has in this field.

Dr. Deryl Hart, Durham, N. C.: I want to report two cases of hemorrhage from the biliary tract, traumatic in origin. The first was in a 15-year-old boy who was in an automobile accident and was carried to the hospital in coma. During the next seven days, according to the report from his doctor, he had gradually increasing swelling of the abdomen and then some diminution in the swelling. On the eighth day at operation a tremendous quantity of bile and a small amount of blood was found in the peritoneal cavity. Drains were inserted, and the doctor estimated that during the next two weeks about five quarts of bile drained from the abdominal cavity. Within 21 days the wound had healed and the boy left the hospital, apparently on the road to recovery. In the thirty-fifth day following the injury, at 3:00 A.M., he was awakened with a severe pain in the upper right abdomen radiating around the costal margin to the back. He was taken to the hospital in shock, was treated by transfusions, and after recovery was allowed to leave the hospital. From that time until the seventy-seventh day following the accident he had four similar episodes, three of which required admission to the hospital and transfusions to bring him out of shock.

He was then sent to the Duke Hospital for further treatment. A gastro-intestinal series was negative except for practically 100 per cent retention in the stomach. There was nothing to explain this and it was not present with subsequent roentgen ray studies.

His original surgeon was contacted and his opinion was that the patient had a peptic ulcer, or possibly a post-traumatic portal thrombosis, causing esophageal varices. Before his first operation in the Duke Hospital he had had, following admission, three episodes of severe pain and bleeding and three episodes of mild pain. At times he vomited blood; at other times he passed it by rectum. At the time of this operation nothing whatsoever was found other than adhesions, and the abdomen was closed. Within the next ten days he had seven episodes of bleeding, some of which were mild and some severe, and he received six blood transfusions. In view of the negative findings at operation and the history of bile drainage following the injury, the question was raised as to whether or not he might be bleeding from the biliary tract. It was thought that this might explain the severe attacks of pain in the upper right abdomen over the liver region, followed after two to ten minutes by signs of shock. During his most severe attack, when his blood pressure dropped to 40/0, he vomited undigested food material with no evidence of blood and later passed large amounts of old blood by rectum, this placing the lesion below the stomach.

At the second operation, with the impression that the blood was coming from the biliary tract, the gallbladder was aspirated and found to be filled with blood. The common duct was opened and was likewise filled with blood. The liquid blood was washed out and the blood clots were removed. A catheter was passed into the hepatic ducts and bright red blood dripped from it. The liver was attached to the abdominal wall anteriorly by adhesions, and it was thought that these might be tenting up a blood-filled cavity, preventing its collapse. It was hoped that if this could be released, and free drainage through the common duct provided, the cavity could collapse and the subscapular rupture might heal. The adhesions were divided, and the common duct was decompressed by continuous drainage. The patient had no further hemorrhage and made an uneventful convalescence.

The second case was that of a 49-year-old woman, operated upon for cholecystitis with stones eight months prior to admission to the Duke Hospital. The surgeon reported that he "had had a great deal of trouble with bleeding and had to take some *deep sutures in the liver*" in order to control the bleeding, which was profuse and required many transfusions on the operating table. The patient remained in the hospital for five weeks. During the next eight months, except for short periods of closure, she had almost continuous drainage through a sinus tract at the drainage site and, on a few occasions, had had some bleeding to the outside through this tract. There was some drainage of bile, but most of this passed through to the intestinal tract and she had not been jaundiced. On occasion she passed tarry stools, and six weeks before admission she had a massive hemorrhage through the sinus tract. Following admission to the Duke Hospital she had a rather severe internal hemorrhage, went into mild shock, and was given a transfusion. Subsequently, she passed what was described as a currant-jelly stool, which was strongly positive for blood. Physical examination showed an area of swelling about 4 to 5 cm. in diameter under the midportion of the incision, and this was tender on pressure. At operation, following careful blood and roentgen ray studies, dense adhesions were located around the drainage tract. As soon as these were freed a laminated blood clot was encountered, and when this was manipulated profuse hemorrhage occurred. Blood sprayed out from between the clot and the wall of this false aneurysm. The clot and bleeding point were relatively inaccessible because of dense adhesions about the clot. Bleeding was partially controlled with packs until the clot was exposed adequately to attempt its evacuation and control of the bleeding point. With evacuation of the clot, we finally gained access to the region of the entrance of the duct into the liver. There the bleeding was coming from an opening in the liver, which would just admit the index

finger. The finger could be passed up into the liver for the length of two phalanges, and the finger plugged the opening completely, thus controlling the profuse bleeding.

We then had the problem of how to control this profuse bleeding. We could not remove the finger long enough to do anything, because the patient's blood pressure would drop to shock level within a matter of seconds. We tried various packs, including fibrin foam and clotting globulin, but all were forced out immediately by pressure of the arterial bleeding; we could not control it by compression of the hepatic artery with the finger in the foramen of Winslow. Finally, a large piece of muscle was taken from the thigh and the cavity was packed full. This muscle pack was held in place by heavy silk sutures passed through the rigid fibrous ring about the opening into the liver, and tied across the opening. It was necessary to give 5000 cc. of blood during the time of the operation in order to maintain a blood pressure adequate to proceed with the operation.

We were very skeptical as to the result, but the patient progressed satisfactorily and 12 days after operation she was ambulatory, but a morphine addict from her long-continued illness. She became very insistent about going home, demanded her release, and left against advice. The patient, her family, and her family physician were warned of the condition and of the danger of the muscle pack "blowing out." They were advised that provision be made for immediate operation and adequate amounts of blood be available at all times, if needed. Five days after she reached home and 17 days following operation, the doctor called stating that she had gone into shock and was in the hospital. He was afraid to operate, and 24 to 36 hours later she died as a result of hemorrhage.

DR. ROBERT M. MOORE, Galveston, Texas: I would like to ask Doctor Blakemore if, in his experience, he has found any explanation for the differing behavior of patients with hematemesis? One sees some who bleed to death rapidly. I believe I have seen two in the past few weeks in whom this would have been the outcome had it not been for balloon tampons. Then one sees other patients who had one violent hemorrhage three years ago or ten years ago, and who have had no trouble since. Is it remission, is it thrombosis of veins, or what is it that makes it possible for there to be these long intervals between bleeding episodes in certain patients?

DR. I. A. BIGGER, Richmond, Va.: I want to mention a very interesting problem with which we were confronted a good many years back, similar to the one mentioned last by Doctor Hart. This was a man 37 or 38 years of age, who had gotten up before daylight and gone out into his backyard and stumbled over a "stob"—a stake driven into the ground to which cattle and horses are tethered. He had received a rather severe injury in his upper right quadrant, and had shown evidence of severe hemorrhage. He had been operated on by a local surgeon who had found a rather extensive laceration of the liver, which had been packed. He became rather severely jaundiced and was quite sick, but was allowed to leave the hospital after a few weeks. Several weeks after leaving the hospital this man had a rather severe gastro-intestinal hemorrhage; this was repeated at intervals for a period of seven or eight months. We were then asked to see him, and we found him to be moderately anemic; his general condition, however, was fair. Roentgen ray of the diaphragm showed definite bulging in the region of the right lobe of the liver. On auscultation over the right upper quadrant in the region of the hepatic artery there was a definite systolic bruit, so we made a tentative diagnosis of traumatic aneurysm of the hepatic artery and suggested operation but did not urge it because of the seriousness of the undertaking. The patient was opposed to operation and we did not insist, as we probably should have done. We assumed that the bleeding was due to formation of varices in the lower esophagus, secondary to pressure on the portal vein by the hepatic aneurysm.

Later he developed an acute febrile episode, became jaundiced; and his local surgeon found evidence of a subphrenic abscess. At operation he found a mass of clot and then profuse bleeding, so he packed it and, a little later, referred him to the Medical College

of Virginia Hospital. It was difficult to get adequate blood into him because after the first few transfusions we regularly had severe reactions. At that time we were not familiar with the Rh factor; I am quite sure now that this man was an Rh negative. We finally decided to attempt ligation of the right hepatic artery and had scheduled him for operation, but he began bleeding and died before we were able to get him in condition for that procedure.

Postmortem examination showed a most interesting situation. There was an aneurysm of the right hepatic artery, which had ruptured intermittently into the right hepatic duct with great loss of blood into the intestinal tract. The right lobe of the liver had undergone a tremendous degree of atrophy and the left lobe of the liver had apparently taken over, as it was considerably enlarged. In retrospect, I believe we could have occluded the right hepatic artery with relatively slight danger and, by operating before, probably could have saved this patient.

DR. ARTHUR H. BLAKEMORE, New York (closing): I want to thank you for this discussion. I never told Doctor King—he spoke of practicing up in the country—that I had one of his playboys up there in March. He does not know about this but all I had to do was threaten him with one of these tubes, just keep it in the room, and he promptly stopped bleeding.

I think Doctor Moore has brought up a very intriguing problem. I am sure everyone has thought a great deal about it. We have a terrific variability in intervals of bleeding in many of these cases and that variability, in itself, has many times misled us regarding therapy. Certainly it has been true to a great extent in cases of portal hypertension secondary to extra-hepatic block, called Banti's syndrome, in relation to splenectomy. Doctor Whipple has told me of many instances in which there was apparent cure by splenectomy; it was only a question of following them long enough and it would recur, many times after the lapse of years. Certainly in the group with normal livers we often find a terrifically high portal pressure by measurement, and we have tried to reason it out on the basis of relation to the blood volume and the red cell mass, which has been true in a certain number of cases. I remember a golf pro who was an outstanding case; he bled for a number of years and kept track of his hemoglobin, and knew that when it got to be 60 he was going to bleed; and he would always turn up. We thought of the problem along that line and there are probably many other factors; that certainly is a factor, we believe, in certain cases with extremely high portal pressure.

Concerning the cirrhotic group who have their first bleeding episode, we are becoming more and more impressed with the feeling that a considerable percentage of those cases have at least a strong hypoprothrombinemia component as well as portal hypertension. We have come to that conclusion because often when a cirrhosis case comes with his first complaint of bleeding, a review of his liver status reveals it to be pretty bad. When you get a chance to check the esophageal varices you will often find them barely discernible and quite small. That same case may not bleed again, and we do not push the idea of doing shunts on those people as the result of just one bleeding episode. We feel that in certain cases the periportal fibrosis will not go on to the point of creating serious portal hypertension and development of large varices. There are other cases where we know that does happen; we have followed several such cases over a period of years, and the second bleeding attack will be purely on the basis of portal hypertension; large varices have developed, liver function tests have improved, and these two groups must be recognized. The ones that bleed the second time certainly have a tremendous tendency to repeat bleeding. There are other angles to it, and it is an interesting problem to contemplate.

DR. HARRY H. KERR, Washington (closing): I want to thank Doctor Hart and Doctor Bigger for their discussion, and to tell you of an incident of which I was

reminded by the aneurysm hemorrhage. A man was brought into Garfield Hospital with a huge mass in the lower left quadrant, in bad shape and with no history. Everyone in the hospital was interested and wondered what it was. Finally one of our surgeons explored it and ran into a dissecting aneurysm of the common iliac. He was suddenly faced with a spurt of blood and he jammed his thumb into the hole. Dr. Frank Hagner was in the operating suite and was called in. The operator said, "You saw this old man; I have run into a dissecting aneurysm of his common iliac, and I don't know what to do." Frank looked the situation over and said, "There is no question about it—amputate the thumb!"

ANNOUNCEMENT

The National Paraplegia Foundation wishes to announce the establishment of a limited number of fellowships for research in spinal cord disease and trauma and in the complications commonly associated with such disease or injury. These fellowships carry a minimum stipend of $3000 per year and may be awarded to any candidate who has demonstrated a capacity for medical research and has outlined a program of meritorious study. The fellowships will be awarded by the Medical Advisory Committee and are open for award for the academic year 1950-1951. Application forms may be obtained from the Chairman of the Medical Advisory Committee, and applications should be submitted to him not later than June 1, 1950.

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